

ENDOMETRIOSIS-ASSOCIATED PAIN, SOCIAL IMPACT, AND INFORMATION THROUGH INTERNET SURVEY

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INAUGURALDISSERTATION
zur Erlangung des Grades eines
Doktors der Medizin
des Fachbereichs Medizin der
Justus-Liebig-Universität Gießen

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vorgelegt von

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1

INTRODUCTION

1.1. Definition

Endometriosis can be defined as the growth of endometrial tissues composed of both glandular and stromal elements at an extrauterine site¹, which can cause dysmenorrhea, dyspareunia, non-cyclical pain and subfertility, whereas endometriomas are cysts of endometriosis within the ovary².

1.2. History of endometriosis

Knapp³ summarized the earlier descriptions of endometriosis in the 17th-18th centuries. The oldest publication about endometriosis can be traced approximately 300 years back to Shroen⁴ in his book called *Disputatio Inauguralis Medica de Ulceribus Ulceri* in 1690⁴. In the 18th century, Roederer⁵ (in his book *de ulceribus utero molestis observationibus*), Broughton⁶, Tailford⁷, Duff⁸, Ludgers⁹, Brotherson¹⁰ and many other authors tried to explain the incidence, characteristics, pathophysiology, signs, and symptoms of these sore lesions. At that time histological knowledge did not exist and they recognized and recorded the examination mostly postmortem. In the late 19th century Diesterweg¹¹ reported a case of polyps of the posterior uterine wall. Indeed, Cullen¹² made his first observation from 100 cases, which he called adenomyoma. In 1894 and 1896 he drew the conclusion that glandular inclusions found in adenomyoma derived from the mucous membrane of the uterus. Von Recklinghausen^{13,14,15} in his 3 publications (1893, 1895 and 1896) made detailed descriptions of adenomyomata. He distinguished between extrauterine and intrauterine adenomyomata. However, in his view only cases arising within the uterine wall possessed the same structure as the uterine mucosa. Iwanoff¹⁶ claimed the first adenomyoma evaluation in his Russian papers. The origin and nature of the endometriosis glands had been discussed differently as early as 1895 by Orloff¹⁷ and

continued by Mayer¹⁸ in 1903. This theory was supported by Schickele¹⁹ in 1904. He stated that the mucosal growth was of mesonephric origin. As late as 1918 Lockyer²⁰ discussed the various theories on the origin of endometriosis found outside the uterine cavity. He considered a serosal origin of this endometriosis in his book. Russel²¹ described endometriosis as adhesions from the broad ligament with the right ovary. Russel²¹ considered the endometriosis tumors as due to the presence of aberrant portions of the Müllerian duct in the ovary. Semmelink and De Joselin de Jong²² in 1905 presented a case of ovarian endometrioma. They decided that the tumor was of Wolffian duct origin. Noris²³ reported the case of a 29-year-old woman with severe pelvic pain. He discussed the possible origin of the endometrial cells and believed that the endometriosis was of Müllerian duct origin.

In 1903 Cullen²⁴ published a summary of 19 cases of adenomyoma of the uterus. This time he was able to determine that in most cases the glands originated from the epithelium lining the uterine cavity. Cullen^{25,26} published other summary papers in 1919 and 1920. He presented a comprehensive review of all his findings, reporting the heterotopic presence of the uterine glands and stroma almost ubiquitously in the lower abdomen, uterus, including the ovary (Figure 11.1). He believed that the uterine mucosa on the surface of the ovary and lower abdomen was due to an overflow of the adenomyoma of the rectovaginal septum. With the knowledge provided by Cullen's research^{12,24,25,26,27}, Sampson^{28,29} in 1921 and 1927 accomplished two publications, which were considered as the discovery of endometriosis and provided the first theory on the pathogenesis of the disease.

Sampson was to contribute more to our knowledge of endometriosis than any other individual before or since, earning him the sobriquet "Father of Endometriosis"³⁰.

1.3. Epidemiology

The actual prevalence of endometriosis in the general population is still unknown³¹, since laparoscopy or laparotomy is required to make a definitive diagnosis. An earlier estimate of the prevalence of chronic pelvic pain (which is the main symptom of endometriosis) in the United States based on audits of referrals to gynecologic clinics, accounts for 2-10% of the outpatient gynecologic consultations and is the indication for approximately 20% of laparoscopies³¹. Based on the few reliable data, the prevalence can reasonably be assumed to be around 2-10%^{32,33,34,35}.

The incidence of endometriosis in Japanese women has been reported to be twice that of Caucasian women³⁶. There is a clinical impression that blacks have lower rates of endometriosis and Orientals have higher rates than whites³⁷ (Table 11.1 - Appendix). About 5% of endometriosis cases are seen in postmenopausal women, which are caused by hormone replacement therapy³⁸. In very rare cases, men undergoing long-term estrogen therapy may also be affected³⁸.

1.4. Pathogenesis and pathophysiology

Up to now, more than three theories of pathogenesis of endometriosis have been proposed:

1. Metastatic theory^{39,40,41,42}.

It is the most widely accepted theory that endometriosis results from metastatic implantation, particularly retrograde menstruation³⁹. This theory also explains the vascular and lymphatic spread of endometriosis. It was suggested for the first time by Sampson in 1940⁴⁰. The theory assumes a transport mechanism of endometrial tissue from the uterine cavity into the peritoneal cavity in a retrograde fashion. The endometrial cells remain viable and implant themselves on the serosal layers. Up to 90 % of normal women have shown bloody peritoneal fluid during the menstrual periods^{41,42}. Some observers showed that the shed of endometrium had

growth potential in vitro and that viable endometrial cells can remain in the peritoneal fluid. Most women have equilibrium between the development of minimal peritoneal lesions and the capacity of the abdominal cavity to resorb the endometrial tissue present in the abdominal cavity.

2. Metaplastic theory^{43,44}

In contradiction to the metastatic theory is the metaplastic theory of serosal surfaces (coelomic epithelium) or Müllerian remnant tissue. This was suggested by Meyer⁴³ in his publication of 1919. Both endometrial and peritoneal cells are derived from the epithelium of the coelomic wall. The theory suggested the possibility of peritoneal cells differentiating into functioning endometrial tissue. According to this hypothesis endometriosis arises as a result from secondary stimulation of inflammation or hormonal influences. Based on studies in the rabbit it is suggested that substances liberated by the endometrium could induce endometriosis-like lesions in the undifferentiated mesenchyma. More recently it is shown that ovarian endometriotic lesions are able to arise as a process of metaplasia from the ovarian surface epithelial/mesothelial cells in the presence of endometrial stromal cells and estradiol⁴⁴.

3. Induction theory⁴⁵

This is a combination of both theories. It suggests that substances released from shed endometrium induce undifferentiated mesenchyma to form endometriotic tissue⁴⁵.

4. Immunological theory^{46,47}

The ability of endometrial implants to survive in ectopic locations may be related to an aberrant immune response. The theory of an altered immune system and endometriosis suggests that changes in cell-mediated immunity and humoral immunity may contribute to the development of the disease⁴⁶. The pathophysiology of immune alteration and endometriosis was depicted by Berkkanoglu and Arici (Figure 11.2 - Appendix)⁴⁷.

5. Environmental theory^{48,49,50,51,52}

In 1993 Rier⁴⁸ and her colleagues found that rhesus monkeys exposed daily to 5 or 25 parts per trillion (ppt) of dioxin for 4 years developed endometriosis, with incidence and severity related to dose. It was also shown in research for deficiency in genes responsible for dioxin detoxification, which may predispose women to endometriosis^{49,50}. Dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin, TCDD) and structurally related congeners (polychlorinated dibenzo-p-dioxins, called dioxins) are families of chlorinated aromatic hydrocarbons (Figure 11.3 - Appendix)⁵¹. Exposure to dioxins occurs mainly through dietary exposure. The pathogenesis of predisposing women to endometriosis is plausible by altered production of various cytokines and growth factors, by remodeling of endometrial tissue through effects on the expression and activity of matrix metalloproteinases and the tissue inhibitors of matrix metalloproteinases, by promoting angiogenesis, or by compromising the immune system⁵².

6. Genetic theory^{53,54,55,56,57}

There is increasing evidence that endometriosis is inherited as a complex genetic trait in which multiple genes conferring disease susceptibility interact with each other and with the environment to produce the phenotype. Research groups worldwide are trying to identify such susceptibility genes through a positional cloning approach⁵³. Evidence for a genetic basis comes from case reports of concordance in monozygotic twins^{55,56} and a study of monozygotic and dizygotic twin pairs from the Australian National Health and Medical Research Council Twin Register⁵⁷.

1.5. Signs and Symptoms

Clinical presentation of endometriosis is associated with a wide variety of symptoms, although in many patients it is asymptomatic. There is no pathognomonic symptom for this disorder, thus making the diagnosis of endometriosis difficult. Most risk factors for endometriosis relate to a concept

of condition that is estrogen-dependent and associated with reflux of menstrual fluid to the peritoneal cavity. The risk of endometriosis seems to be dependent on the amount of menstrual flow. Endometriosis is more common in women with a short menstrual cycle (≤ 27 days), and longer menstrual flow (≥ 7 days) and spotting before onset of the menses^{58,59,60}. A decreased likelihood of endometriosis has also been observed in women who have been pregnant. The risk of endometriosis is inversely related to the number of pregnancies^{61,62}. A positive family history of endometriosis is relevant since there is growing evidence suggesting that a genetic component plays a role in endometriosis, probably involving a polygenic pattern of inheritance^{63,64,65}. There is significant familial clustering, and first degree relatives of women with endometriosis have a sevenfold greater chance of having endometriosis^{66,67}. Associations between red hair, dysplastic nevi and endometriosis have been reported^{68,69}.

The most important symptoms of endometriosis are infertility and chronic pelvic pain. In the population of infertile women undergoing surgical intervention, the rate of endometriosis is higher than in fertile control women (14%)³¹. But the prevalence of infertile women among the endometriotic patients has not been precisely evaluated. In women with pelvic pain, endometriosis was detected at the time of surgery in 19%³¹. The pelvic pain typically consists of dysmenorrhea, intermenstrual pain and dyspareunia. Although dysmenorrhea is not predictive of endometriosis, it is the most commonly reported symptom, and its severe form is highly suggestive of endometriosis⁷⁰. Dysmenorrhea is usually progressive, with the onset of pain often preceding the onset of menstrual flow. It usually continues throughout the menses and occasionally persists for several days afterwards. The pain is most often localized in the lower abdomen and deep pelvis. It is bilateral, often radiating to the back and thighs. It is often described as dull and aching and may be associated with rectal pressure, nausea and episodes of diarrhea⁷¹. Intermenstrual pain may exist after the dysmenorrhea, and in very severe cases patients may suffer from pain throughout the cycle. Endometriosis-related dyspareunia is usually positional and most intense upon deep penetration.

Dyspareunia was found more in the rectovaginal (100%) form than in the ovarian (77%) or peritoneal form (88%)⁷². It is most intense prior to menstruation, but in severe cases it may preclude intercourse throughout the month. Dyspareunia is usually associated with endometriosis of the cul-de-sac and rectovaginal septum⁷³.

Endometriosis has been found in extrapelvic organs (e.g. intestinal tract, urinary tract, surgical scars, lungs, thorax, peripheral nerves and the central nervous system). Consequently, patients may have symptoms with cyclic and menses-aggravated cyclic bleeding and inflammation. Hepatic endometriosis may present with cyclic right-sided subcostal pain. Endometriosis of the urinary tract can cause hematuria, dysuria, urgency and frequency of urination. Involvement of the ureter may cause flank and iliac fossa pain due to partial ureteric stenosis. Pleural and pulmonary endometriosis may be manifested by hemophthysis, chest pain, and shortness of breath. Cerebral endometriosis can lead to perimenstrual headaches or even seizures⁷⁴.

Symptomatic endometriosis after the menopause is rare and usually related to hormone replacement therapy⁷⁵. Nevertheless, cases of de novo endometriosis in postmenopausal women have been described⁷⁶.

1.6. Diagnosis

The currently available diagnostic tools have not only advantages but also limitations. Despite an extensive research for new laboratory tests and advances in imaging technologies, at present there are no simple noninvasive diagnostic tests and endometriosis still remains an enigmatic condition.

a. Physical examination

Physical findings for endometriosis are nonspecific. Pelvic examination should be performed during the menses because the sensitivity of the examination is higher than at any other time during the menstrual cycle^{1,31}.

b. Radiologic evaluation

Not unexpectedly, radiologic evaluation of small endometriotic implants is limited. Therefore, the radiologic findings play an important role in identifying and evaluating an endometriotic cyst³⁹.

b.1. Ultrasonography^{31,39,77,78,79,80}

The role of ultrasonography is limited to detecting endometriotic cysts of the ovary but not adhesions or superficial implants^{31,39,77,78}. However, both transabdominal and transvaginal approach should be performed.

Transabdominal ultrasound is useful to detect bladder or abdominal wall endometriosis. Transvaginal ultrasound should be performed preferably to evaluate the cul-de-sac and cysts. The diagnostic accuracy of ultrasound has been reported to have up to 92% sensitivity and 99% specificity^{79,80}.

b.2. Doppler examination⁸¹

There is controversy regarding the vascular presence of endometriomas. Alcazar⁸¹ found that in patients with pelvic pain, vascularization of ovarian endometriomas is higher and the pulsatility index is lower than in asymptomatic patients. Improvement in diagnostic accuracy may be achieved with the introduction of power Doppler, which allows detection of low-velocity flow.

b.3. Three-dimensional ultrasound^{82,83}

Applications of three-dimensional ultrasound in detecting cystic ovarian tumors have been reported^{82,83}.

b.4. Magnetic resonance imaging^{39,84,85}

MRI has been shown to have greater specificity for the diagnosis of endometriomas than other noninvasive imaging techniques.

Occasionally it may also visualize solid endometriotic implants and adhesions because of better visualization of the surrounding anatomic structures. In addition to using routine T1-weighted and T2-weighted pulse sequences, a T1-weighted fat-suppressed sequence should be performed to accentuate the difference in tissue signal.

Endometriomas have relatively homogenous high signal intensity

(similar to or greater than fat) on T1-weighted images. With removal of surrounding fat, the recognition of conspicuous lesions is improved. Lesions with degenerated blood products, including methemoglobin and concentrated protein, appear with high-signal intensity areas on T1- and T2-weighted images. A common and important feature of an endometrioma is “shading” (loss of signal within the lesion), which can be seen on T2-weighted images³⁹. Togashi et al.⁸⁴ found that a “definitive” diagnosis of an endometrioma was made when a cyst was hyperintense on T1-weighted images and shading on T2-weighted images (sensitivity of 90% and specificity of 98%).

MRI demonstrates high sensitivity, specificity, positive and negative predictive values, and accuracy in predicting the locations of extension of disease in patients with deep pelvic endometriosis⁸⁵.

c. Tumor markers^{86,87}

An elevated CA-125 (cancer antigen 125) level in peripheral blood has been described. Several studies performed in a population at high risk for endometriosis have demonstrated that serum CA-125 has good specificity (86-100%) but poor sensitivity (13%)⁸⁶. Table 11.3 (Appendix) shows a summary of multiple markers for endometriosis (from Bedaiwy⁸⁷).

d. Laparoscopy⁸⁸

Up to now, laparoscopic assessment in combination with histological examination remains the gold standard for the definitive diagnosis of endometriosis. More than 60 years ago, Sampson^{28,29} described pelvic endometriosis by using terms such as red raspberries, purple raspberries, blueberries, blebs and peritoneal pocket. Knowledge of the most common location of endometriosis is nowadays required for accurate visual inspection of the pelvic and abdominal cavity during laparoscopy. The typical appearance of endometriosis is often made up by classical powder burn, puckered black or bluish lesions⁸⁸. There are three different forms of endometriosis that must be considered in visual inspection during

laparoscopy: peritoneal implants (Figure 11.4 - Appendix), endometriomas (Figure 11.5 - Appendix), and deep infiltrating lesions (Figure 11.6 - Appendix). The latter nodules are difficult to examine during laparoscopy. However, meticulous palpation using the laparoscope probe may identify these lesions.

On the other hand, lesions associated with hemangiomas, old sutures, necrotic areas from ectopic pregnancies, cancer cells, epithelial inclusions, residual carbon from previous laser surgery, hysterosalpingogram dye reaction and inflammatory cyst may be mistaken for endometriosis.

e. Pathology

The classic endometriotic lesion has a diffuse mixture of glands, stroma, intraluminal debris and fibromuscular scarring. It may be confused with fibrotic tissue from previous inflammatory disease or postoperative scarring in white lesions of endometriosis.

f. Staging of endometriosis.

The American Society for Reproductive Medicine has published a revised classification of endometriosis in 1997⁸⁹. It is shown in Figure 11.7 - Appendix.

Keckstein⁹⁰ has proposed a new scoring system called “ENZIAN-Score” as an addition to the r-AFS Score for deep infiltrating endometriotic lesions.

1.7. Differential diagnosis

Differential diagnosis of endometriosis is grouped according to the organ system^{1,91}:

- a. Genital area: pelvic inflammatory disease, pregnancy complication, adnexal masses
- b. Gastrointestinal tract: hernia, abdominal wall trigger points, irritable bowel syndrome, lactose intolerance, constipation, gastrointestinal malignancy, diverticulitis, diverticle
- c. Urology: interstitial cystitis, bladder stone

- d. Orthopedics: fibromyalgia, spondylosis, hernia of the nucleus pulposus
- e. Pelvic pain of undetermined etiology (tension from pelvic muscle, eg. cramp of the levator or piriform muscle), psychological factors.

1.8. Treatment

The efficacy of medical and surgical treatment of endometriosis is a source of questions and controversies. A complete resolution of endometriosis is not yet possible⁹². Moreover, ectopic endometrium can proliferate under hormonal influence after a long time without estrogens⁹³. Therefore, therapy should be directed to three essential outcomes: reduction of pain, increasing of the pregnancy rate, delay of recurrence as long as possible⁹².

a. Medical therapy

Medical therapy plays a role in the therapeutic strategy when administered over a prolonged period of time. Given their good tolerability, minor metabolic effects and low cost, progestogens must therefore be considered as drugs of choice and are currently the only safe and economic therapy to surgery⁹⁴.

a.1. Danazol

Danazol is a derivative of 17 α -ethinyl testosterone. The recommended danazol dosage for treatment is 600 to 800 mg/day. Although a small number of studies of lower dosage of danazol show relief of endometriosis-associated pain⁹⁵, the use of danazol is of limited value⁹⁶.

a.2. Progestogens

The mechanism of progestogens is to decidualize the endometrial tissue followed by atrophy. There is evidence suggesting that another mechanism of action at the molecular level is the suppression of angiogenesis and matrix metalloproteinases, enzymes that are important in the implantation and growth of ectopic endometrium⁹⁷. The most extensively used progestogen is medroxyprogesterone acetate (MPA). The dose ranges from 20 mg to 100 mg daily and 150

mg as 3 monthly depots⁹⁶. Side effects are generally well tolerated (e.g. breakthrough bleeding due to hypoestrogenemia, nausea, breast tenderness, fluid retention, depression)⁹⁸. Breakthrough bleeding can be corrected by short-term administration of estrogen⁹⁸ or increase of the progestogen dose⁹⁶. Other progestogens, e.g. levonorgestrel, can be utilized via an intrauterine delivery system and are effective for the treatment of rectovaginal endometriosis⁹⁹.

a.3. Oral contraceptives (combination estrogen-progestogens)

The mechanism is believed to decidualize the endometrial tissue and followed by atrophy. Oral contraceptives suppress proliferation and increase the abnormally low apoptotic activity of the endometrium of women with endometriosis^{94,100}. Moreover, anovulation, decidualization, amenorrhea and the establishment of a steady estrogen-progestogen milieu contribute to the quiescence of disease.

a.4. GnRH agonist

Gonadotropin-releasing hormone (GnRH) agonists are modified forms of GnRH that bind to the pituitary GnRH receptors and remain for a long time. They are thus identified by the pituitary as rapidly pulsatile GnRH, and after initial stimulation of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretions, result in a down-regulation of pituitary gonadotropin secretion. The end result is a lack of ovarian stimulation and a hypoestrogenic milieu similar to the postmenopausal situation. It is also postulated that the GnRH agonist alters plasminogen activators and matrix metalloproteinases, factors important in the development of endometriosis¹⁰¹. The side effects include complaints in the postmenopausal situation (e.g. hot flushes, decreased libido, breast tenderness, insomnia, depression, irritability, osteoporosis, and decreased skin elasticity). A modification of GnRH agonist treatment is to add back small amounts of steroid hormone, based on the theory that the estrogen level needed by endometriosis is higher than that of estrogen needed by the brain, bone and other tissues¹⁰².

- a.5. Gestrinone (ethylnorgestrienone, R2323, an antiprogesterone steroid)⁹⁶
- a.6. Mifepristone (progesterone antagonist) and selective progesterone receptor modulators (progesterone agonist-antagonist)⁹⁶
- a.7. Selective estrogen receptor modulators (Raloxifene)⁹⁶
- a.8. GnRH antagonists⁹⁶
- a.9. Aromatase inhibitors (e.g. anastrozole)⁹⁶
- a.10. Other experimental medication⁹⁶

With a growing understanding of the pathogenesis of endometriosis, more precise molecular targets for treatment have been identified (e.g. TNF- α inhibitors, angiogenesis inhibitors, pentoxifylline, matrix metalloproteinase inhibitors). Thus, these medications are still under development and promise a greater efficacy and flexibility than traditional treatments.

b. Surgical management

Because of the lack of prospective, randomized and controlled studies, firm conclusions regarding optimal treatment are difficult¹⁰³. The treatment objectives are to restore normal anatomy, to remove or ablate endometrial implants, and to prevent or delay recurrence of the disease. Surgical treatment has been more commonly effected by the laparoscopic approach since the development of advanced laparoscopic equipment and operative techniques. In moderate or severe endometriosis with anatomic distortion of the pelvis, surgical treatment is still the first line treatment to maintain or restore fertility.

Surgical principles

The principle in surgical treatment is the removal of all endometrial implants in an atraumatic, hemostatic fashion in the least amount of time. Adhesions are excised rather than simply lysed because of the possible presence of endometriosis within adhesions. Reduction of tissue desiccation and maintenance of a clean surgical field are facilitated by copious irrigation with physiologic fluids. The operative success rate

correlates with meticulous surgical techniques that maintain serosal integrity and decrease the risk of de novo formation of adhesion.

Adamson¹⁰³ has summarized the surgical principles in the treatment of endometriosis (Table 11.4 - Appendix). Although the laparoscopic approach is preferred for surgery, it is always important to obtain the best result even by performing a laparotomy if necessary. Elimination of endometrial implants may be accomplished by laser ablation, electrosurgical dissection or sharp resection.

c. Pre- and postsurgical management

In case of minimal or mild endometriosis-associated infertility, the use of coagulation, laser, excision or adjuvant medical therapy in combination with laparoscopic surgery is still under debate¹⁰⁴. Laparoscopic destruction was proven to be the first line therapy¹⁰⁵. In case of moderate and severe endometriosis-associated infertility, medical therapy alone is not effective. In a study of 814 women with ovarian endometriomas, the authors obtained a cumulative pregnancy rate of 51% after combined treatment with GnRH-agonist and laparoscopic surgery. The pregnancy success occurred within 10 months after surgery¹⁰⁶.

In case of endometriosis-associated pain, surgical treatment alone has an unsatisfactory result in treating the pain. But medical treatment alone has also an unsatisfactory result in the management of pain. Waller¹⁰⁷ reported that the cumulative recurrence rate for the five years after 6 months of GnRH-agonist alone therapy was 53.4% (36.9% for minimal disease and 74% for severe disease). Therefore, postoperative adjuvant medical treatment, causing hypoestrogenism and amenorrhea might delay the recurrence of symptoms^{108,109}.

d. Alternative therapy (complementary care)

An increasing number of women with endometriosis are turning to complementary or alternative therapies. They experience relief of the symptoms with modifications to their diet, lifestyle changes, naturopathic remedies, and self-nurturing behavior (yoga, massage, qi gung,

acupuncture). These activities help them to achieve a sense of control over their lives and a reversal of the control that endometriosis had over them¹¹⁰.

Ayurveda

Ayurveda is one of the oldest therapeutic methods. It comes from the ancient Hindus and might still be applicable in western medicine. Its therapeutic concept is based on 5 ground elements: air, wind, fire, water and earth¹¹¹.

Homeopathy

In the 18th century, Dr. Samuel Hahnemann pioneered homeopathy in Germany. He discovered chemical substances that act in healthy humans as poisons but in pathologic situations (diseases and disorders) act as medications¹¹².

Acupuncture

It is based on traditional Chinese medicine (TCM). In acupuncture it is believed that the needles correct any imbalances in the flow of life force along meridians. In contrast, many western medical, nursing and physiotherapy staff believe that the needles stimulate the nervous system in a particular way. Acupuncture may also produce effects through local changes in the tissues, e.g. stimulating blood flow. Acupuncture and acupressure appear promising for dysmenorrhea but further studies are still needed¹¹³.

1.9. Social support for patients with endometriosis

Chronic endometriosis is notoriously difficult to treat and many women become frustrated with their health¹¹⁴. In an endometriosis center treatment must be integrated in one concept. Extended knowledge about the medical treatment and experienced operators (laparoscopy) must be the first requirements for an endometriosis center. Adding a cooperation venture between the gynecologist, a patient support group, and the Endometriosis Association would complete the whole therapy concept. These patients should be encouraged to develop a supportive network of friends, family and co-

workers. The most supportive sources tend to be other women with the same disease, endometriosis¹¹⁰.

1.10. Problems in endometriosis

Women with chronic pelvic pain, infertility and dysmenorrhea try to search for information about their problems. They should get reliable and competent information and have early awareness to search medical help. This information can be transferred passively by media, papers, internet, etc, or be delivered by relatives, friends, even directly by the medical staff. The information should be reliable, accurate, up-to-date, easy to understand, and available in many public medical centers. It takes time to analyze and discuss information until the women make their decision, whether they continue to find medical help. After the decision making, most of them continue to visit a medical expert. Decision is becoming more difficult as they have to decide whom they have to consult. The surgeon, internist, gynecologist or urologist may come to be a choice. After hearing the first opinion of one expert, most women are going to another specialist to obtain a second opinion. Finally, these women come to a gynecologic practice. Here we must face the fact that the diagnosis of endometriosis remains challenging. The “gold standard” diagnostic tool still is laparoscopy with histological examination.

The uncertainties surrounding the diagnosis and management of endometriosis often leave the patient in pain, feeling confused by the limited information provided by her doctor and with a mixed bag of emotions: fear, grief, anger and a feeling of self-guilt being prominent among them¹¹⁵. An open, mutually understanding relationship between doctor and patient is necessary if the diagnosis is to be made without undue delay. Appropriate management will then include that the doctor takes time to explain the condition and its associated uncertainties, to discuss the treatment options, and to forewarn about possible side-effects¹¹⁵.

Therefore, women affected by endometriosis claim that delayed diagnosis is a great problem¹¹⁶. Some studies have shown that the delay in diagnosis of endometriosis is around 7 years (Table 11.6 - Appendix). Ballweg¹¹⁷ has summarized that the delay in the diagnosis of endometriosis (from over 7000 confirmed cases) is on average more than 9 years. Nevertheless, endometriosis is a major problem and current treatments are far from satisfactory¹¹⁷. Misdiagnosis and underdiagnosis of endometriosis are not only due to the limitations of diagnostic tools but also to a lack of recognition of the symptoms by the patients and physicians³¹.

The impact of endometriosis, a disease that already produces intense symptoms, is worsened by a current lack of understanding of the disease beyond its pelvic definition¹¹⁷. Denny¹¹⁸ conducted a study to explore women's experience of endometriosis. Despite the existence of severe pain, their symptoms were frequently trivialized or normalized. The pain is huge and often described as overwhelming or intense and can only be managed with over-the-counter pain killers. There were also instances of vomiting or fainting when the pain was at its worst. Dyspareunia was experienced as a sexual difficulty and could strain the relationship and marriage. In the work and social relationship endometriosis also has negative effects. Women explained that their social life was curtailed because they missed many social events. They expected more support from friends and family to understand their condition. The experiences in the workplace were quite diverse. Living with severe pain usually entailed taking some sick leave, or being unable to perform the job adequately, while the taking of strong analgesics limited the type of work they could do. Women with endometriosis must face the fact that they have to resign from work¹¹⁸.

The economic correlation between chronic pelvic pain and endometriosis has also been reported by a few studies^{119,120,121,122}. In the United Kingdom, Davies¹¹⁹ estimated the annual costs of intractable gynecologic pain at £158.4 million for women with either endometriosis or no recognizable disease.

Mathias¹²⁰ calculated that the annual direct cost for visits to the physician because of chronic pelvic pain was estimated to be \$881.5 million.

Beyond all of these problems, help for women with chronic pelvic pain, dysmenorrhea, infertility or even endometriosis is needed. This help should include: right and current information, correspondence with other women with the same problems, discussion with experts. These three points must be available anytime and anywhere and should also be supported by many experts. Nowadays, the preferable platform is an internet Web site. Through an internet Web site, information can be accessed 24 hours a day, connected to other endometriosis-based Web sites, and is easy to update. Information about the definition, symptoms, signs, examinations, treatments, and rehabilitations should be provided. A possibility to communicate with experts could also be a satisfaction. The doctors, nurses, and other health providers are the persons who introduce the Web sites to their patients. The patients are sensitized to the Web sites through brochures, seminars, invited to “Health Talks”, and by advertisement in the private praxis. During surfing and browsing the internet Web sites, the visitors are asked to participate actively in a discussion, chat forum, teleconference, and correspondence with one or more experts. They try a so-called endometriosis test through Web sites. With this test, the possibility of endometriosis is predicted by collecting the symptoms and signs of patients. They would get a reply after finishing the test and thereafter the attention about the seriousness of their problems will arise. These women seek the health providers earlier to consult about their endometriosis-associated complaints.

One way of patient information about endometriosis, based on an internet Web site, is www.endometriose.de. Here, women can get information about endometriosis. Information about the diagnosis, symptoms, signs, therapy, seminars, and social groups are explained and discussed in detail. On this Web site the browsers can fill out a questionnaire called “EndoTest”. This test is aimed at collecting the women’s common complaints and at predicting the possibility of endometriosis derived from the severity of the problems. At the

end of the questionnaire, the assessment of quality of life, encompassing physical, psychological and social aspects, can be obtained.

Increasingly, consumers access the internet for information about their health problems and treatments. Some browse the internet only to learn more about their health care. The information provided at health Web sites, unfortunately, is often inaccurate, incomplete, or biased, and may even evoke a potential risk to the person's health^{123,124,125}. In recent studies, many tools were developed to evaluate health-related Web sites, e.g. HITI¹²⁶, HON Foundation¹²⁷, URAC's Health Web Site Accreditation¹²⁸, Criteria developed by the American Public Health Association¹²⁹ and the American Medical Association¹³⁰. Seal approval would be given to the Web site meeting the standards for health information. With major search engines (Lycos, Yahoo, Google, Netscape) more than 900.000 Web sites were found¹³¹ (Accessed on September 26, 2004). To date, there are limited studies to evaluate and examine the quality of Web sites on endometriosis. In this paper, 20 Web sites on endometriosis were evaluated based on standard criteria in assessing the quality of health information on the internet.

2**QUESTIONS**

It is the aim of this investigation to collect more information in the area of endometriosis-associated pain and its social impacts. Since the internet has become a very popular medium to easily and anonymously access forums and chat rooms with specific topics, research was undertaken to find out information about those searching advices and also what specific information is wanted. The following questions have been specifically investigated:

1. What kind of information do women with pelvic pain, dysmenorrhea, infertility, and dyspareunia need while searching medical help?
2. How many women in the studied population have chronic pelvic pain and what is the level of pain?
3. How many women in the studied population have dysmenorrhea?
4. How many women in the studied population have dyspareunia?
5. And how many women in the studied population have infertility?

And further questions about the impact of these problems:

6. How far do these problems interfere with the quality of life?
7. How far do these problems interfere with productivity?
8. How big is the economic burden from endometriosis-associated impacts?
9. How many women can be suspected to have endometriosis as the cause for their pelvic pain on the basis of the symptoms?
10. What kind of information about endometriosis is provided on Web sites?
11. Which Web sites meet the standard criteria and are appropriate for most patients?

3

MATERIAL AND METHODS

A Web site for endometriosis, www.endometriose.de, has been developed in order to provide online-information for the public. On this site complete information on endometriosis is available. The page is mainly written in German and it has also a feature to switch the language into Greek, English, Turkish, Polish, and Russian. Every single language has at least one special contact partner who understands the language well. The browser is welcomed with a banner “When you have abdominal pain, menstrual pain with infertility, it could be caused by endometriosis“. Moreover, the preface tries to show how important endometriosis is to women who have periodical pain and chronic abdominal pain. At the end of the preface, the readers are reminded that this information is an additive to consultation of the physician.

On the further sites, visitors can read more details about endometriosis. Definition and pathogenesis are described in detail and without using any medical terms. The two main theories about the pathogenesis of endometriosis are discussed. The readers are expected to realize that the cause of endometriosis is still unknown and that the environment and life style could play a big role in the pathogenesis. On the next page, the main symptoms of endometriosis are shown, which are mostly abdominal pain and infertility. The abdominal pain includes cyclic pain (dysmenorrhea), pain during sexual activity (dyspareunia), and chronic abdominal pain. A check list of the pain rhythm is available to help women in the preparation before consultation of the physician. The explanations of the pathogenesis of endometriosis in infertility are also discussed. The readers are sensitized to know more about the main problems in infertility and not to forget that the cause of infertility may be on the male side. The diagnosis of endometriosis is also explained in clear detail, beginning with anamnesis, gynecologic examination, ultrasound examination of the pelvis, and laparoscopic diagnosis. Three therapy options are discussed, including surgical, medical and alternative therapies. Laparoscopic and laparotomic approaches by different techniques using scissors, high frequency instruments, and lasers are discussed as surgical therapy. Rehabilitation is integrated

in the whole management of endometriosis, and most rehabilitation measures are undergone after surgical treatment has been finished. At the end of the journey the browsers can find the names of 14 experts who supported the Web site (List of names is shown in Table 11.7 - Appendix).

Neither registration before nor entering password and login name are needed to browse the whole Web site. It can be accessed 24 hours a day and 7 days a week. On the main page the latest news and the latest programs from the European Endometriosis Information Center (EEIC) are displayed. 241,393 visitors were registered from May 2003 until September 2004. The complete register is shown in Table 11.8 - Appendix. In this study the data is limited to 29 July 2004.

3.1. Data input

3.1.1. Discussion forum

On the main page of www.endometriose.de, the visitors are invited to join the discussion forum by a banner “ask directly our experts in Online Forum”. The patients can address their questions either directly to a specific reference or just at a pool. From this pool, the questions are then distributed to 14 different references. One expert is responsible to answer the questions in one month.

The correspondent may choose the topic by herself, and with the help of this topic she can write the questions. With permission from the respondent the questions can be accessed by the others with a search engine. The topics of discussion, chosen by the EEIC are:

1. Lower abdominal pain
2. Infertility
3. Hormonal therapy
4. Surgical therapy
5. Alternative therapy

6. Follow-up after operation
7. Diagnostics
8. Sterility
9. Pain therapy

Not only one question may be addressed in one letter; most of the letters contained a series of questions with information about the previous history. Open questions are generally used. The responsible experts for the month answer the questions in detail, individually, and within a short time. The experts can ask questions in return if more information is needed from the patients. Other people seeking a similar answer can get the published forum directly through the search engine. Husbands may also write in the discussions forum if their wives have endometriosis problems. Published discussions can be found by an internal search engine. By searching the topic and clue question, discussion themes can be easily found.

Each correspondence letter is summarized based on the core of the question and its answer. It is classified into subgroups. These subgroups are shown in Table 3.1.1.

Table 3.1.1. Subgroups of discussion themes

Main groups	Subgroups
Abdominal pain	Pain treatment Bowel or bladder endometriosis and distant metastasis Psychological effects
Infertility	Chance of pregnancy Pregnancy under hormone therapy Fertility after surgical therapy
Hormonal therapy	Side effects Tailoring of hormonal therapy
Surgical therapy	Indication of surgical treatment Tailoring of surgical treatment
Follow-up	Follow-up after surgical therapy Follow-up after medical treatment
Alternative therapy	
Diagnostics	
Abnormal bleeding	
Endometriosis center	
Cost and insurance	
Recurrence	
Pathophysiology and pathogenesis	
Miscellaneous	

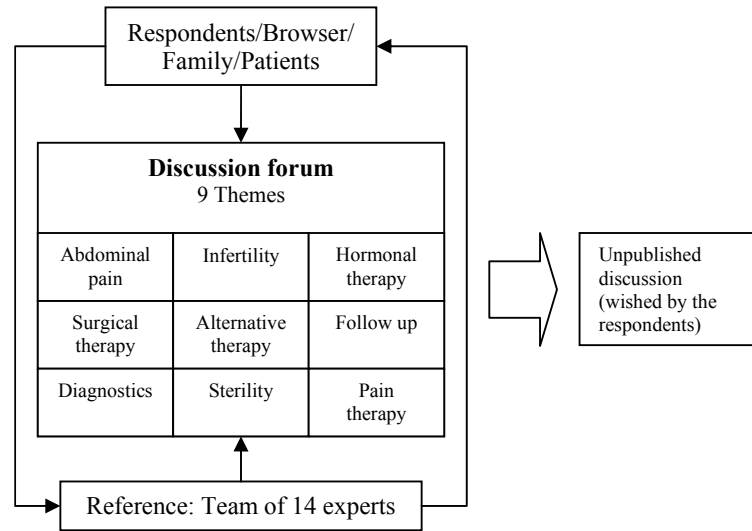


Figure 3.1.1. Flow chart classification of discussion forum

3.1.2. Questionnaire

At the beginning of the Web site, respondents are warned again that this test can only suggest the presence of endometriosis without giving any diagnosis. The respondents are also advised to consult the gynecologist when they have any symptoms or complaints. Endo-Test is not aimed to prove a diagnosis of endometriosis, but when the diagnosis is not achieved this test should be a guide leading to the diagnosis of endometriosis.

The guidelines to fill out the questionnaire can be seen on the first page at the beginning of the Endo-Test. At the end, the test is calculated and the respondents obtain the result directly. They can give their email address if the report of the test is requested.

A total of 12 closed questions was developed and prepared as a questionnaire in HTML format. Respondents click the buttons for each point of the questions. The first part of the questionnaire includes 6 questions which refer to symptoms and signs of endometriosis. The

respondents can continue the Endo-Test by pressing the “Analyze” button or erase the form. The computer calculates the score. Raw scores for this questionnaire were derived from an unpublished study by Bühler et al. Based on the total number of points the respondent gets directly the calculated probability of endometriosis according to her complaints. Table 11.5. (Appendix) presents the scoring process and translated questionnaire.

In the second part of the Endo Test the respondents are asked about the impact of their complaints, signs, and symptoms on their social activities. They can ignore the second part of the questionnaire.

Overall, the Endo Test is aimed at warning the candidate of endometriosis by bringing together her chief complaints, symptoms and the relevant social effect. The questionnaire contains the following items:

1. Questions about signs and symptoms of endometriosis (dysmenorrhea, severity, timing, frequency, dyspareunia, hematuria, hematochezia) in the first part of the questionnaire
2. The relation and possibility of these complaints with endometriosis (infertility, contraceptives)
3. The impact on the candidate’s social activities (energy-vitality, interference of pain with sexual activity, physical activity, days of reduced activity, reduced productivity at work and time of work lost).

Scoring system

Only the first part of the Endo Test was scored. The score system is mostly based on the relation of the symptoms, that given by the respondents, to endometriosis. The most important symptoms of endometriosis are dysmenorrhea, chronic pelvic pain, dyspareunia, and infertility. Endometriosis-associated dysmenorrhea is usually

progressive, continues throughout the menses, and the onset of pain often precedes the onset of menstrual bleeding. Therefore, always having dysmenorrhea, pain before the onset of menstrual bleeding, and most pain together with the bleeding are associated with a higher score. Chronic pelvic pain without any other gastrointestinal problems is also associated with endometriosis. The score for frequent chronic pelvic pain is higher. Dyspareunia is usually positional and intense upon deep penetration. Dyspareunia at the entrance of the vagina is not associated with endometriosis, therefore 0 point.

Endometriosis in extrapelvic organs is associated with cyclic and menses-aggravated cyclic bleeding from the affected organ. Taking contraceptive pills is in this case related to hormonal treatment in endometriosis.

However the correlation between questionnaires and clinical diagnosis of endometriosis should be proven in a further study.

3.1.3. Evaluation of Web sites on endometriosis

Major search engines have been identified: Yahoo, Google, Netscape, Excite, AltaVista, MSN, and Lycos. Key words and phrases (endometriosis) were then used in each of the search engines. Using the combinations, each search engine was evaluated for the relevance of the first 20 sites. Relevant URLs were highest selected when the key phrase “endometriosis” was used. The Yahoo and AltaVista search engines yielded a significant number of relevant URLs (897,000 hits and 902,000 hits, respectively) and were chosen as the two search engines to be used. This method of identifying Web sites for evaluation was consistent with study from Oermann et al.¹⁶⁰. Web sites for professional purposes, such as continuing education sites, were excluded from this search method. Duplicates on the search engines were eliminated, and the selection continued down the list for a total of 20 sites on both search engines. The American Medical Association (AMA)¹³⁰ has published guidelines for medical information on the

internet. In our study, the quality of 20 Web sites was assessed according to objective scoring scales adapted from the AMA online health information guidelines. These objective scoring scales were introduced by Huang¹⁵⁹. They divided three evaluation criteria (Web site ownership, editorial content, and navigation) into subcriteria, and gave a score of 1 for each criteria met. There are 7 criteria regarding Web site ownership and affiliations, 8 criteria regarding editorial content, and 11 criteria regarding navigation. The complete criteria are shown in Table 11.11. Web sites with and without seal approval from international standards for health information (e.g. HON, URAC's) were compared. The twenty Web sites on endometriosis identified by the search engines Yahoo and AltaVista are shown in Table 3.1.3. The most relevant Web sites are listed first, followed by other similar pages.

Web sites in this study were classified based on total scores into poor, average and good. A score of 0 to 8 was categorized as poor, a score from 9-17 was categorized as average, and a score of more than 18 (maximally 26) was categorized as good.

Table 3.1.3. List of 20 endometriosis-associated Web sites

1.	www.endometriosis.org
2.	www.hcgresources.com/endoindex.html
3.	familydoctor.org/handouts/476.html
4.	www.ivf.com/endohtml.htm
5.	www.womensurgerygroup.com/conditions/endometriosis/overview.asp
6.	www.endometriospaintreatment.com
7.	www.womensendosurgery.com/endometriosis.html
8.	www.emedicine.com/emerg/topic165.htm
9.	www.endofacts.com
10.	www.endocenter.org
11.	www.endozone.org or www.endometriosiszone.org
12.	endometriosis.allbio.org
13.	www.endometriosisasn.org
14.	www.centerforendo.com
15.	www.nlm.nih.gov/medlineplus/endometriosis.html
16.	www.endo.org.uk
17.	www.endometriose.de
18.	www.endo101.com/index.htm
19.	www.endometriosis.com
20.	www.womenshealthchannel.com/endometriosis/index.shtml

3.2. Statistical analysis

All data were administered by Mr. Max Meyn (meyn@blitz.de) in Bamberg, who is also the webmaster of www.endometriose.de. From the main data bank, records of discussion forum were transferred into comma delimited document (csv) and records of Endo-Test were transferred into text format (txt). Both CSV file and TXT file were converted into database using SPSS version 12 for Windows.

To examine the bivariate association between two variables, cross-tabs with Pearson's chi square test were used. The association between total score and endometriosis-associated social impact was tested using the one way ANOVA test by comparing the change scores. In terms of probability of endometriosis, the categories of endometriosis score and severity of social impact were tested with cross-tabs and Pearson's chi square. The differences were considered statistically significant if $p < 0.0001$.

For comparison between Web sites, the one way ANOVA test was used. Results were expressed as mean and the increase was statistically analyzed. The differences were considered significant if $p < 0.05$.

4

RESULTS

4.1. Data analysis

4.1.1. Discussion forum

Within 32 months (15 January 2002 until 29 July 2004) there were 2202 correspondence letters written to the experts. Most of the letters were written by those who had problems with endometriosis or symptoms of endometriosis. Only small numbers of men were writing for their wives, and some correspondents even wrote about other themes (outside endometriosis). Examples: letter number 130 on 15 April 2002 was written by the husband of a woman with endometriosis, and letter number 199 on 20 May 2002, karoass@ asked about the Pap Smear Test.

Because there was no standard for writing these letters, respondents were free to formulate their questions. The previous history might be a good clue to explain the problems and help the expert in answering the questions. The age of the correspondents was not always mentioned in the letters.

Table 4.1.1.1. Activities of the references

Name of the references	Frequency	Percent
andreas.ebert@	135	6.13
buehlerfam@	240	10.90
edgardewitt@	112	5.09
gunther.goeretzlehner@	199	9.04
hans-rudolf.tinneberg@	231	10.49
joerg.keckstein@	114	5.18
lmettler@	225	10.22
martin.sillem@	234	10.63
michel.mueller@	78	3.54
regidor@	145	6.58
schindler@	106	4.81
schweppe@	254	11.53
thomas.roemer@	129	5.86
Total	2202	100

The most active correspondents were:

Table 4.1.1.2. The most active respondents

Email address	Frequency of questions
heike.kuemmel@	11
baerbel.daub@	11
yvonne.sagan@	10
ralobe@	9
gwohllleber@	8
mumie2001@	8
ELubke@	7
viviente@	6

Based on the email address (where the correspondents live) demographics can be predicted (Table 4.1.1.3).

Table 4.1.1.3. Demographics of the correspondents

Email address	Country of origin*	Frequency	Percent
.ag	Antigua and Barbuda	1	0.05
.at	Austria	59	2.67
.be	Belgium	2	0.09
.ch	Switzerland	75	3.40
.com	International	430	19.52
.de	Germany	1535	69.70
.edu	Educational organization	1	0.05
.es	Spain	1	0.05
.fr	France	1	0.05
.info	Organization	2	0.09
.it	Italy	7	0.31
.li	Liechtenstein	2	0.09
.lu	Luxembourg	5	0.23
.net	Network system	62	2.81
.nl	Netherlands	3	0.14
.no	Norway	1	0.05
.org	International organization	4	0.18
.pl	Poland	1	0.05
.pt	Portugal	1	0.05
.renault	Company	4	0.18
.ru	Russian Federation	1	0.05
.sg	Singapore	1	0.05
.uk	United Kingdom	3	0.14
Total		2202	100

* Source: <http://www.iana.org/cctld/cctld-whois.htm>

The length of the questions was counted per characters by Excel for Windows XP. The result was calculated by SPSS for Windows version 12. The mean letter had a total of 827 ± 596.71 characters.

Table 4.1.1.4. Maximal and mean length of correspondence letters

	N	Maximum	Mean	SD	Minimum
Length of questions	2202	5285	827	596.71	19
Length of answers	2202	2931	473	340.83	0

Table 4.1.1.5. The most frequently chosen themes

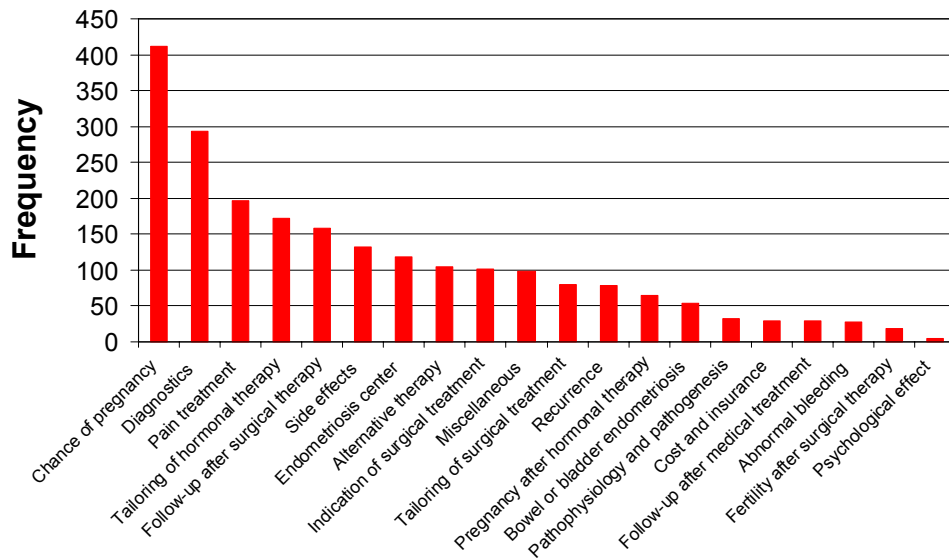
Themes	Frequency	Percent
Alternative therapy	86	3.91
Diagnostics	198	8.99
Hormonal therapy	476	21.62
Sterility	42	1.91
Infertility	483	21.93
Follow-up after operation	137	6.22
Surgical therapy	224	10.17
Pain therapy	71	3.22
Lower abdominal pain	485	22.03
Total	2202	100

The most frequently asked questions were:

Table 4.1.1.6. The most frequently asked questions based on the core questions

Subgroups	Frequency	Percent
Abdominal pain		
• Pain treatment	197	8.95
• Bowel or bladder endometriosis and distant metastasis	53	2.41
• Psychological effect	5	0.23
Family planning		
• Chance of pregnancy	411	18.66
• Pregnancy after hormonal therapy	64	2.91
• Fertility after surgical therapy	18	0.82
Hormonal therapy		
• Side effects	132	5.99
• Tailoring of hormonal therapy	172	7.81
Surgical therapy		
• Indication of surgical treatment	102	4.63
• Tailoring of surgical treatment	80	3.63
Follow-up		
• Follow-up after surgical therapy	158	7.18
• Follow-up after medical treatment	29	1.32
Alternative therapy	104	4.72
Diagnostics	294	13.35
Abnormal bleeding	28	1.27
Endometriosis center	118	5.36
Cost and insurance	29	1.32
Recurrence	78	3.54
Pathophysiology and pathogenesis	32	1.45
Miscellaneous	98	4.45
Total	2202	100

Figure 4.1.1.1. Distribution of the most frequently asked questions



Subgroups of discussion themes

The chance of pregnancy in association with endometriosis was the most frequently asked question (19%). The patients were concerned about their fertility especially after the diagnosis had been made.

Sample questions from patients of this group were:

1. Is pregnancy made more difficult by endometriosis?
2. How much time do I have to become pregnant?
3. Do I still have any chance to become pregnant?

Signs, symptoms, and how to diagnose endometriosis was an interesting topic. 13 % of the respondents wrote about their main complaints and asked the experts about the possibility that they had endometriosis. Most of them had not undergone laparoscopy for the diagnosis of endometriosis. Sample questions were:

1. I have menstrual pain since my first period. I have read about endometriosis in the newspaper. I am afraid that I might have it.
2. Half a year ago my menstrual bleeding became more extensive and I have more intensive menstrual pain although I take contraceptives. How could endometriosis be diagnosed or excluded?

3. Can endometriosis be diagnosed only by laparoscopy or is there any other method to diagnose it?

Information about pain treatment was asked by 8.9% of the respondents. Respondents saw the pain as indescribable and frustrating. It is interesting to note the question:

“What can I do? What happens when the pain does not go away? I do not know how I could begin my story.... 5 years ago endometriosis was diagnosed by laparoscopy, after that I had hormonal therapy for 6 months. So far I have had 3 laparoscopies with hormonal treatment. The pain has not diminished but is even worsening, and I have more and more pain. It influences my daily life in spite of a shorter treatment interval”.

Tailoring of the hormonal therapy was asked for by 7.8 % of the respondents. The main discussion in this topic concerned the best hormonal therapy, the dosage of the hormone, alternative therapy to hormones, schedule of therapy, and length of therapy. Samples of questions:

1. I have been told to take mini-pills for 3 months. Is this right?
2. I have been told to take Diane (contraceptive pill) for 3 months. Would you also advise me to take this medication?
3. Which medication is better to treat endometriosis, Cerazette or Valette?

7.2 % of the respondents inquired about the follow-up after surgical therapy. They wanted to know the next treatment after the operation, the time to begin hormonal therapy, the duration of hospitalization, second look operation, and rehabilitation. Samples of questions were:

1. Is it possible to obtain rehabilitation after finishing all therapies for endometriosis?
2. Once they told me to undergo hysterectomy and finally have another hormonal treatment.... now they told me to undergo

oophorectomy. I want to know what is going to happen to me after that.

3. How long is the recovery time after hysterectomy?

Side effects of medical treatment for endometriosis were asked by 6% of the respondents. Samples of questions were.

1. I am going to have a series of injections to put me into the climacteric phase. What is the side effect of this medication?
2. I have been given Yasmin (contraceptive pill) since the operation. Now I have no pain at all but I feel always sick, nauseous and hypoglycemic. Could it be the side effect of the hormone?
3. Could a cyclic depression be related to endometriosis alone or also to the hormone treatment?

5.4 % of the respondents considered endometriosis centers near their residence as an important information. They had their own gynecologist, but they felt it was better to have the entire treatment in an endometriosis center. They asked whether the experts could tell them a name or center in their neighborhood.

It was apparent that the psychological factor played a big role in endometriosis. 5 respondents asked questions about this psychological factor. These questions were:

1. I suffer from anxiety and emotional changes before my menstruation. Is this known also in endometriosis?
2. Which psychological background plays a big role in endometriosis e.g. sexual abuse?
3. Could dizziness be a result of endometriosis?
4. Every month before my menstruation I have nasal bleeding for 4-5 days. Interestingly it happened every month just before the menstruation. Could it be also endometriosis? My ENT doctor said it may only be a psychological factor.

5. May endometriosis cause a personality change on account of the extreme pain?

4.1.2 Questionnaire

All participants in this study had voluntarily filled out the questionnaire. They were recruited over a range of 12 months from 09 July 2003 until 29 July 2004. From them, 10665 respondents were recruited who filled out the questionnaire. As shown in Figure 4.1.2.1, the questionnaire was divided into 2 groups of questions. The first part (questions 1 to 5) asked about the signs and symptoms of endometriosis. Question 6 asked more about the medication, whether the respondents were taking oral contraceptives. It was obligatory to fill out this part completely in order to get the total point leading to the probability of endometriosis. In this case 10665 respondents completed questions 1 to 6. From the second part of the questionnaire (questions 7-12), information about the social impact of the pelvic pain as main symptom of endometriosis could be retrieved. It was not compulsory to complete the second part. Therefore only 45% of the questions 7-12 were completely answered.

4.1.2.1. Distribution of answers

Questions 1-6

As shown in Table 4.1.2.1.1, the end result showed that the questionnaires were almost completely filled out by women who had dysmenorrhea (97%). The respondents experienced dysmenorrhea in different ways. 68% said they had dysmenorrhea in all menstrual bleedings, 20% said only occasionally, and 9% stated that painful menstrual bleeding was rare. The onset of pain together with the beginning of menstrual bleeding was recorded for 52% of symptomatic dysmenorrhea individuals. In addition, 48% of symptomatic

respondents claimed that they experienced dysmenorrhea days before the menstrual bleeding.

74 % of the respondents found that the most painful time of the menstrual period was the onset of bleeding. Only 26% of the respondents experienced this extensive pain before the menstrual bleeding. Dysmenorrhea since the menarche was reported by 44% of all 10332 dysmenorrheal individuals. More than half of dysmenorrheal women (56%) stated that dysmenorrhea came after the menarche.

Chronic pelvic pain was reported by 7616 respondents (71%). Only 29% had no pelvic pain at all. The distribution of chronic pelvic pain was varied, the intensity of pain ranging from extensive to mild. Extensive pelvic pain was reported by up to 43% of women with chronic pelvic pain. Dyspareunia was also recorded in 61% of all respondents. Within the dyspareunia group, 75% agreed that the pain depended on the coital position. Pain at the entrance of the vagina was reported by 13%, followed by 35% for pain in the pelvic area, and 52% for pain in the deep vagina. Interestingly, hematuria or hematochezia was claimed by 19% of the respondents. Infertility was an important subject by presenting the problem in 39% of all questionnaires. Among the total respondents only one fifth (21%) took contraceptive pills.

Table 4.1.2.1.1. Result of the questionnaires

Questions	Answers	Frequency	Percent	Total
1. Do you have painful periods?	Always	7275	68.21	10665
	Occasionally	2157	20.23	
	Rarely	900	8.44	
	Never	333	3.12	
1.1. If yes, when does the pain begin in your period?	Days before the menstrual bleeding	4939	47.80	10332
	With the menstrual bleeding	5393	52.20	
1.2. If yes, when do you have the most pain?	With the menstrual bleeding	7621	73.76	10332
	Before the menstrual bleeding	2711	26.24	
1.3. If yes, have you had this pain since the first time you had your period?	At menarche	4693	45.42	10332
	After menarche	5639	54.58	
2. Do you have lower abdominal pain monthly without having any menstrual period and you do not have any gastrointestinal problem?	Often	2591	24.29	10665
	Sometimes	5025	47.12	
	Never	3049	28.59	
2.1 If yes, is this pain very deep and strong or only mild?	Extensive	3295	43.26	7616
	Light	4321	56.74	
3. Do you also have pain during intercourse?	Yes	6479	60.75	10665
	No	4186	39.25	
3.1. If yes, does it depend on the position at intercourse?	Yes	4924	76.00	6479
	No	1555	24.00	
3.2. If yes, where is the center point of this pain?	Deep in the vagina	3370	52.01	6479
	In the pelvic area	2250	34.73	
	At the entrance of the vagina	859	13.26	
4. Do you also have bleeding with urination and bowel movement before or during menstruation?	Yes	2047	19.19	10665
	No	8618	80.81	
5. Do you have infertility Problems?	Yes	4179	39.18	10665
	No	6486	60.82	
6. Are you currently taking any contraceptives?	Yes	2250	21.10	10665
	No	8415	78.90	

Questions 7-12

4882 women gave information about alteration of their quality of life. The majority of respondents (51%) thought that their quality of life had been extremely reduced by the pain. While 12% had no alteration in their quality of life, 37% thought there was a moderate change in their quality of life. Extreme limitation of sexual activity was reported by 36% (1754 respondents). Another 37% saw only mild problems during intercourse, and the rest (27%) saw no problem at all in sexual activity. Respondents generally (90%) appeared to be restricted in their daily activity by the menstrual pain. 60% of them even had extreme

restriction during their menstrual period. Only 10 % of them had no restriction at all in their physical activity. 51% of the respondents found that work performance was also decreased utmost by menstrual pain. Only 14% found no change in work performance and 35% agreed that there was only a modest effect on it. The restriction in work performance, obtained from the majority of respondents (64%), could be prolonged from one to three days in every menstrual bleeding. Impairment in the work place up to more than 3 days was reported by 1133 respondents (24%). Only 594 women (12%) were working normally without limitation during the menstrual period. The total loss of working time in a year ranged from less than one day, two to ten days and more than ten days off work. 4815 respondents gave information about the time lost. Contrary to the impairment of work during menstrual pain, 58% of the women had taken only one day off in a calendar year of work during their menstrual cramp episode. Only 28% (1352 respondents) and 14% (653 respondents), respectively, had to stay at home more than 2 days because of their pain.

Table 4.1.2.1.2. Result of the questionnaires

Questions about	Answers	Frequency	Percent	Total
Quality of life	Extreme	2503	51.27	
	Moderate	1801	36.89	
	No effect	578	11.84	4882
Sexual activity	Extreme	1754	36.13	
	Moderate	1806	37.20	
	No effect	1295	26.67	4855
Physical activity	Extreme	2889	59.49	
	Moderate	1490	30.68	
	No effect	477	9.83	4856
Productivity	Extreme	2451	50.39	
	Moderate	1718	35.32	
	No effect	695	14.29	4864
Days of impairment	>3 days	1133	23.45	
	1-3 days	3105	64.26	
	0 day	594	12.29	4832
Days of absence in a year	>10 days	653	13.56	
	2-10 days	1352	28.08	
	0-1 day	2810	58.36	4815

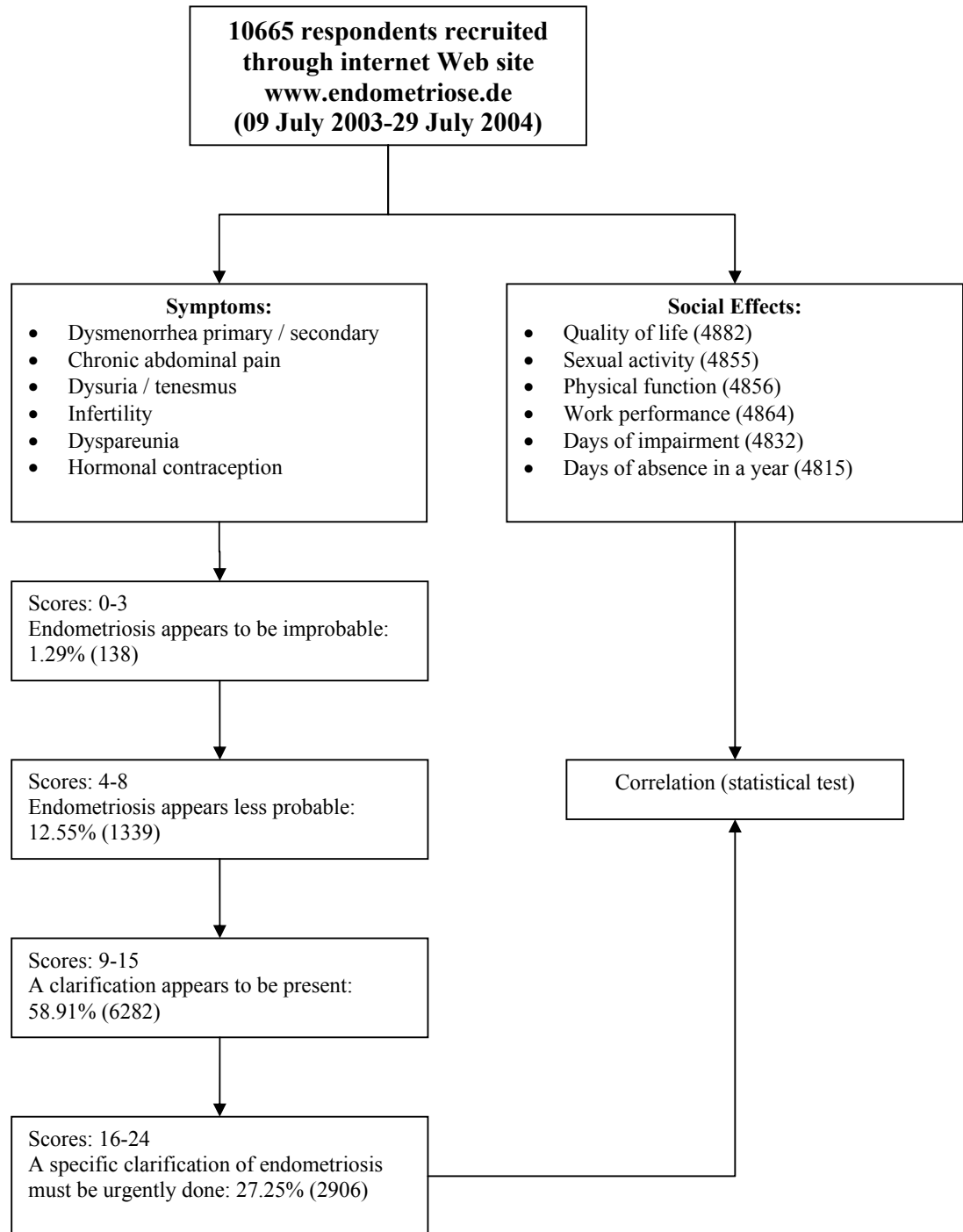


Figure 4.1.2.1. Flow chart of scoring system from Endo-Test

4.1.2.2. Scoring system

With the scoring system developed by Bühler, the entire questionnaire was evaluated. Based on symptoms and signs of endometriosis (questions number 1 to 6), the possibility of endometriosis was classified into 4 categories. Endometriosis appears to be improbable with a total of 0 – 3 points and less probable when the score reaches 4 – 8. With scores up to 9 – 15, endometriosis appears to be probable. With scores up to 16 – 24, endometriosis should be highly suspected, and specific procedures leading to the diagnosis of endometriosis should be performed.

The distribution of the total score can be seen in Table 4.1.2.2.1. The mean of total points is 12.89 ± 3.98 . 59% of all respondents could be categorized as suspect of endometriosis (9–15 total points). 27% of the respondents could be categorized as apparently highly suspect of endometriosis (16-24 points). A specific clarification of endometriosis was strongly advised in this category. Only 2% was included in category one as improbability of endometriosis and 12% for a lesser probability of endometriosis.

Table 4.1.2.2.1. Distribution of total score for the prediction of endometriosis

Total score	Prediction	Frequency	Percent
0	Improbable	41	0.38
1	Improbable	30	0.28
2	Improbable	35	0.33
3	Improbable	32	0.30
4	Less probable	41	0.38
5	Less probable	79	0.75
6	Less probable	197	1.85
7	Less probable	458	4.29
8	Less probable	564	5.29
9	Appears to be probable	750	7.03
10	Appears to be probable	861	8.07
11	Appears to be probable	869	8.15
12	Appears to be probable	941	8.82
13	Appears to be probable	917	8.60
14	Appears to be probable	986	9.25
15	Appears to be probable	958	8.98
16	Specific clarification need	823	7.72
17	Specific clarification need	740	6.94
18	Specific clarification need	539	5.05
19	Specific clarification need	366	3.43
20	Specific clarification need	232	2.18
21	Specific clarification need	116	1.09
22	Specific clarification need	58	0.54
23	Specific clarification need	23	0.22
24	Specific clarification need	9	0.08
Total		10665	100

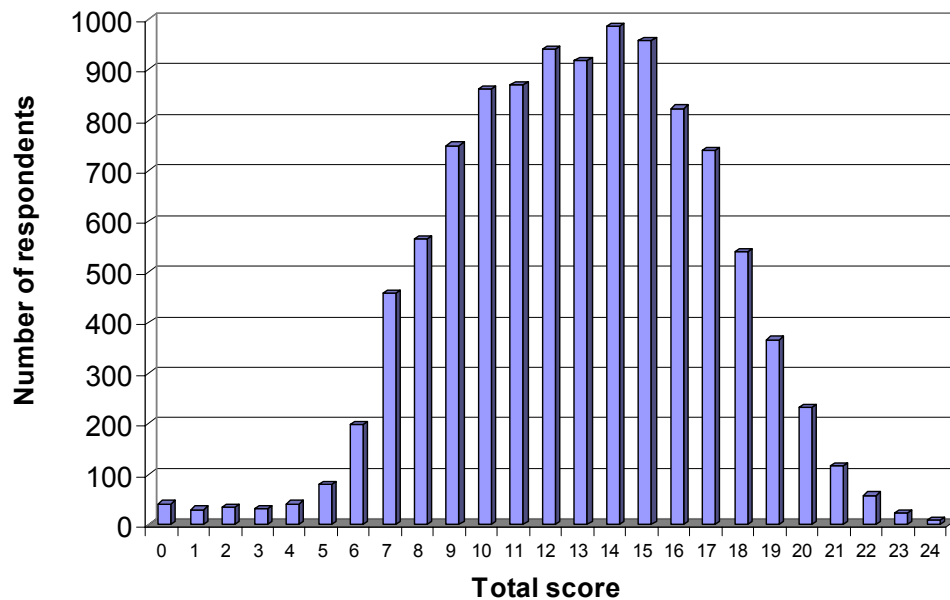


Figure 4.1.2.2.1. Distribution of total score

4.1.3. Web site comparison

The first 20 results from both search engines (Yahoo and AltaVista) are similar. The complete address was shown in Table 11.10 - Appendix. The overall scores for the three scoring scales were average. The mean score for the overall score was 14.

Web site ownership information

The source of the information is considered a marker of quality and enhances the credibility of the Web site. Regarding the Web site ownership information, 80% of Web sites clearly indicated information about ownership and affiliation. However, only 55% showed copyright information of specific content. Moreover, only 45% of Web sites asked about registration and password protection. Information about payment subscriptions, document delivery and viewing was provided only by 45% (9) of all 20 Web sites. The complete distributions are shown in Table 11.10 - Appendix.

Editorial content

Regarding the quality of the Web site content, 65% of Web sites listed all staff members and individuals responsible for content quality. However, only 35% of Web sites reviewed the content for quality, including originality, accuracy, and reliability by either peer review or editorial boards. As for the timeliness of the Web contents, only 15% posted the date of the content publications and revisions. The sources of specific contents were noticed only in 30% of the Web sites.

Navigation of Web contents

Regarding the navigational function, 60% of Web sites provided the search engine for their own Web contents. 50% of Web sites offered customer service information, which included the so-called internet consultation. But only 40% of Web sites featured frequently asked

questions. PDF files and software download navigation was integrated in 60% of the Web site. Most Web sites were easy to navigate through functional internal-external links and allowed viewers to return to a previously browsed Web page.

There were 8 Web sites (40%) which received the HON certificate. The HON logo was placed on the Web site. Only 2 Web sites (10%) belonged to the government. 6 Web sites (30%) were managed by foundations, e.g. Europäisches Endometriose Informations-Centrum (EEIC), Endometriosis Associations, Endometriosis Research Center, etc. And 6 Web sites (30%) were sponsored by a private company, e.g. profit internet provider, pharmaceutical company.

4.2. Statistical analysis

4.2.1. Questionnaire

From a total of 18 questions (12 main questions, and 6 sub-questions), 153 correlations could be combined. The pattern of total scores can be found in Table 4.1.2.2.1 and Figure 4.1.2.2.1.

Dysmenorrhea

Respondents with continuous dysmenorrhea reported more frequent chronic pelvic pain ($p < 0.0001$) than respondents with less dysmenorrhea. There was a significant increase in the intensity of pelvic pain with increased frequency of dysmenorrhea ($p < 0.0001$). Another result indicated that women with continual dysmenorrhea were more likely to have dyspareunia, more likely to have rectal or urinary bleeding, more likely to have infertility but did not take contraceptive pills ($p < 0.0001$). The summary of the correlation between dysmenorrhea with other endometriosis-associated symptoms is shown in Table 4.2.1.1.

As expected, there was a significant correlation between dysmenorrhea and quality of life. 32% of the respondents without dysmenorrhea had no change in their quality of life, whereas in severe dysmenorrhea groups an extreme change in the quality of life was reported by 60% of the respondents. Respondents with more frequent dysmenorrhea had a significant likelihood of staying in bed or missing work on more than 10 days per year ($p<0.0001$). Table 4.2.1.3 shows the correlation between dysmenorrhea and social impact.

Dyspareunia

Regarding dyspareunia there was a tendency that respondents with more frequent dysmenorrhea were more likely to have dyspareunia ($p<0.0001$). As expected, dyspareunic women had difficulties in their sexual life. 48% of the respondents with dyspareunia even had extremely limited sexual activity ($p<0.0001$). But dyspareunia alone had no significant relationship with infertility ($p=0.204$). A summary of the correlation between each parameter is shown in Table 4.2.1.2.

Social impact

The correlation between social impacts with endometriosis-associated symptoms was tested by the chi square test.

Quality of life in respondents with more frequent dysmenorrhea was extremely reduced. 60% of respondents reported an extremely reduced quality of life and having dysmenorrhea all the time. Dysmenorrhea in this group was characterized by the onset of pain days before bleeding. Dysmenorrhea since menarche ($p=0.08$) and the most painful day during the menstrual bleeding ($p=0.003$) were not significantly related with the quality of life. Respondents with extreme changes in the quality of life more often had extensive chronic pelvic pain, dyspareunia, infertility, hematuria, and hematochezia ($p<0.0001$).

Extreme limitation of sexual activity was reported by 1754 respondents. Sexual activity was also extremely limited by always having dysmenorrhea, frequent and extensive chronic pelvic pain, dyspareunia, infertility, hematuria and hematochezia.

Productivity was also restricted by endometriosis-associated symptoms, and these changes were reported by 4864 respondents (46%).

Respondents with more frequent dysmenorrhea tended to have a higher restriction of productivity ($p<0.0001$). Chronic pelvic pain influenced productivity also significantly ($p<0.0001$).

The most important quantitative indicators for the social impact of endometriosis were reduced-activity days, and time lost from work. Almost half of the respondents (45%) gave this information. Days of impairment by endometriosis-associated pain ranged between 0, 1-3 and more than 3 days, and time lost from work was indicated by days of absence in a year ranging from 0-1 day, 2-10 days, and more than ten days. Respondents who had more than three reduced-activity days during their menstrual pain had a tendency to have dyspareunia, more frequently dysmenorrhea, more often chronic pelvic pain, hematuria or hematochezia, and the use of oral contraceptives ($p<0.0001$).

Dysmenorrhea in this group was characterized by onset some days before the bleeding, and the maximum painful time being before the time of bleeding. Chronic pelvic pain in respondents with more than three reduced-activity days was described as extreme pain.

14 % of 4815 respondents who gave information about time lost from work stated that they were absent from work more than 10 days a year. These respondents reported more frequent dysmenorrhea, more extensive pelvic pain, a tendency to have dyspareunia, hematuria or hematochezia ($p<0.0001$), but not infertility ($p=0.007$) and use of oral contraceptives ($p=0.029$). Indeed, dysmenorrhea was characterized only with its onset days before the time of bleeding ($p<0.0001$).

Total score

The total score could be related by using the ANOVA test with social impact. A significant correlation could be also found between categorization of the sum score and the social data.

In the quality of life group there was a significant reduction of the quality of life with a higher probability of endometriosis ($p < 0.0001$). Twelve percent of the respondents recalled no change in the quality of life, and had a mean score of 11.37 ± 3.22 . Increased total scores were found significant for respondents with lower quality of life. 2503 respondents with extremely poor quality of life had a mean score of 14.43 ± 3.54 .

This was also to be expected for the sexual activity group. Reduction of sexual activity was significantly correlated with intensified probability of endometriosis ($p < 0.0001$). Women with no change of their sexual life had a mean score of 11.12 ± 2.96 , whereas women with a moderate disturbance had a mean score of 13.60 ± 3.23 and with severe disturbance a mean score of 15.18 ± 3.35 . The mean scores of these respondents increased significantly ($p < 0.0001$) with the level of disturbance in their sexual activities.

Respondents with a higher probability of endometriosis score had also more disturbances in their physical activity, and this correlation was statistically significant ($p < 0.0001$). 4856 respondents reported reduction of physical activity during menstrual pain which ranged between 'no effect', 'moderate', and 'extreme'. The mean score of respondents with moderate limitation was 12.89 ± 3.38 . A significant score change was calculated for women with extreme physical limitation (mean: 14.19 ± 3.49).

By using the ANOVA test productivity was correlated with total score. Extreme limited productivity was reported by respondents with the highest probability of endometriosis ($p < 0.0001$). Moderate restrictions had mean scores of 13.29 ± 3.40 , while extreme restrictions reached mean scores of 14.19 ± 3.55 .

No respondents (0%) with the lowest probability of endometriosis (score 0–3) had given information about disability in their work for more than 3 days during their menstrual pain (Table 11.9 – Appendix). And 544 (37%) from a total of 4832 respondents with maximal endometriosis score had reported that they were disabled in work for more than 3 days because of their menstrual pain. This correlation was statistically significant ($p < 0.0001$). Analysis showed that respondents who had work limitations for more than 3 days during their menstrual cycle had a significantly higher score ($p < 0.0001$).

Comparison between the yearly days of absence with the total of points (Table 4.2.1.5) showed that the total scores of respondents who had more than 10 days of absence from work in a calendar year were significantly higher than those of respondents with less than 10 days of absence ($p < 0.0001$).

None of the respondents with an endometriosis score between 0–3 were disabled for more than 2 days. The proportion of respondents with overall lost working time of more than 10 days per year significantly increased in groups with a higher endometriosis score ($p < 0.0001$). 296 respondents had reported lost working time for more than 10 days and had the highest probability of having endometriosis.

Table 4.2.1.1. Correlation of dysmenorrhea with other endometriosis-associated symptoms

Dysmenorrhea	Chronic pelvic pain (%)			Severity of pelvic pain (%)		Dyspareunia (%)		Rectal or urinary bleeding (%)		Infertility (%)		Oral contraception (%)	
	Never	Sometimes	Often	Extensive	Light	No	Yes	No	Yes	No	Yes	No	Yes
Never	52.55	30.03	17.42	71.17	28.83	47.75	52.25	88.29	11.71	65.77	34.23	71.17	28.83
Seldom	41.67	43.44	14.89	69.5	30.44	47.00	53.00	87.44	12.56	65.11	34.89	69.56	30.44
Sometimes	31.90	50.95	17.15	76.40	23.60	42.14	57.86	82.43	17.57	63.00	37.00	76.40	23.60
Always	24.89	47.22	27.89	81.15	18.85	37.04	62.96	79.16	20.84	59.41	40.59	81.15	18.85
Chi square test:	p<0.0001			p<0.0001		p<0.0001		p<0.0001		p<0.0001		p<0.0001	

Table 4.2.1.2. Correlation of dyspareunia with infertility and sexual activity

Dyspareunia	Infertility (%)		Sexual activity (%)	
	Yes	No	Moderate	Extreme
Yes	39.67	60.33	12.36	40.04
No	38.44	61.56	31.75	47.60
Chi square test:	p=0.204		p<0.0001	

Table 4.2.1.3. Correlation between dysmenorrhea and social impact

Dysmenorrhea	Quality of life (%)			Sexual activity (%)			Physical activity (%)			Productivity (%)			Impairment days (%)			Absence days yearly (%)		
	No change	Moderate	Extreme	No change	Moderate	Extreme	No change	Moderate	Extreme	No change	Moderate	Extreme	0	1-3	>3	0-1	2-10	>10
Never	32.00	46.00	22.00	36.00	36.00	28.00	86.96	8.70	4.34	83.33	6.25	10.42	76.6	14.9	8.5	91.3	4.3	4.4
Rarely	40.42	40.07	19.51	41.75	31.93	26.32	44.56	43.51	11.93	56.99	36.02	6.99	49.5	42.8	7.8	88.4	8.5	3.1
Occasionally	24.62	50.76	24.62	34.83	38.72	26.45	18.45	53.58	27.97	30.39	40.06	21.55	24.7	62.5	12.8	79.5	17.3	3.2
Always	6.39	33.32	60.29	23.50	37.27	39.23	4.16	24.66	71.18	6.36	32.71	60.93	5.8	66.9	27.3	50.7	32.4	16.9
Chi square test:	p<0.0001			p<0.0001			p<0.0001			p<0.0001			p<0.0001			p<0.0001		

Table 4.2.1.4. Mean of total score from social impact questions

	N	Mean	SD
Quality of life			
No effect	578	11.37	3.22
Moderate	1801	12.90	3.31
Extreme	2503	14.43	3.54
Total	4882	13.50	3.58
Sexual activity			
No effect	1295	11.12	2.96
Moderate	1806	13.60	3.23
Extreme	1754	15.18	3.35
Total	4855	13.51	3.58
Physical activity			
No effect	477	11.23	3.37
Moderate	1490	12.89	3.38
Extreme	2889	14.19	3.49
Total	4856	13.50	3.57
Productivity			
No effect	695	11.58	3.31
Moderate	1718	13.29	3.40
Extreme	2451	14.19	3.55
Total	4864	13.50	3.58
Impairment days			
0 day	594	11.71	3.46
1-3 days	3105	13.25	3.39
>3 days	1133	15.16	3.49
Total	4832	13.51	3.58
Absence days in a year			
0-1 day	2810	12.86	3.43
2-10 days	1352	14.18	3.48
>10 days	653	14.96	3.70
Total	4815	13.51	3.58

Table 4.2.1.5. Correlation of probability of endometriosis with absence days in a year

Absence days (n=4815)	Category of sum score (probably of endometriosis)			
	0 – 3	4 – 8	9 – 15	16 – 24
0 – 1 day	9 (0.32%)	265 (9.43%)	1883 (67.01%)	653 (23.24%)
2 – 10 days	0 (0%)	71 (5.25%)	777 (57.47%)	504 (37.28%)
> 10 days	0 (0%)	30 (4.59%)	327 (50.08%)	296 (45.33%)
Pearson's chi-square test:				p<0.0001

4.2.2. Web site comparison

Most of the Web sites (60%) were classified only as average. Only 30% of them were categorized as good Web sites. The mean score for the 20 endometriosis Web sites was 14.

Web sites which place a HON Certificate on their sites were compared with Web sites without HON certificate. Web sites with a HON Certificate had higher scores (11.83 vs. 18.13, $p<0.05$) than Web sites without the HON Logo.

5

DISCUSSION**Internet Consultation**

The proportion of publications about patients searching for medical information in the internet is limited. Few data are available to date on the subject of internet use of study for such purpose, and the study available that sheds some light on this question is a European study by Coulter and Magee¹³². Jeannot¹³³ has also reported about patients' use of the internet for health care in Switzerland. It showed that only 10 % of respondents used the internet to find medical information¹³³. Another study was performed in the USA by Diaz¹³⁴ and showed that almost 53.5% of patients visiting 5 general internists used the internet for medical information. Those using the internet for medical information were more educated¹³⁴. Hufken¹⁸¹ had tried to find out the internet use for health information among the German population. He found through computer-assisted telephone interviews that approximately 50% of 2026 respondents used the internet to look for advice or information about health or health care.

Over a period of 16 months, the homepage www.endometriose.de recruited 237,159 visitors. The discussion forum, as part of www.endometriose.de, was attended by 2202 respondents. The Endo-Test was filled out by 10,665 respondents. We considered the report of Hufken¹⁸¹ that round 50% of German patients are using the internet for medical information and counted our respondents to predict how many people dealt with endometriosis. We reached a number of 474,318, a very large number of patients with endometriotic problems. Based on statistical data in 2003 from the Statistisches Bundesamt Deutschland¹⁸², there were about 17,417,000 women living in Germany, aged 15 to 45 years. With an endometriosis prevalence of 2-10% among the general population, about 350,000 to 1,741,000 women in reproductive age are probable to have endometriosis.

Limited details have been reported about the information needs of women with endometriosis, particularly when this information was collected through an internet site. The importance of using the internet as a source of medical information has become

increasingly popular as more patients “go online”. According to a survey in the United States, 93 million adults (80% of adult internet users) have used the World Wide Web to obtain health or medical information¹³⁵. By 2005, an estimated 88.5 million adults will use the internet to search for health information and / or health-related products and to communicate with providers¹³⁶. Access to a large amount of medical information is available through an estimated 20,000 to 100,000 health-related Web sites¹³⁷.

The finding of this study showed that as many as 411 (19%) of the participants focused their endometriotic problem on the chance of pregnancy. Half of them were trying to become pregnant or had infertility problems and had already undergone IVF (in vitro fertilization) therapy. Some of them were frustrated because their family planning could not be fulfilled. Here, support groups play an important role in educating the patients, in changing perception about endometriosis, and as media for counseling and the sharing of experience.

Secondly, how to diagnose endometriosis was a great problem for the patients (13%). The main question from this group was “Do I have endometriosis?” and this question would be followed by “is laparoscopy or laparotomy the only possibility for the diagnosis of endometriosis?” At present there are no simple noninvasive diagnostic tests and endometriosis still remains an enigmatic condition³¹. Although direct assessment of endometriotic foci at laparoscopy may be viewed as a “gold standard” for identifying endometriosis, the correlation of laparoscopic observation with histological findings is often poor.

Thirdly, treatment of pain was an important subject in the discussion forum. Most of the respondents were frustrated by untreatable pain. Taking pain killers is not a solution for these patients. Correct indication for surgery, tailoring of the surgical treatment according to the patient’s needs, would be the next question of the entire treatment. Many treatment options are nowadays available, such as hormonal treatment with medroxyprogesterone acetate¹³⁸, oral contraceptives¹⁰⁰, goserelin plus anastrozole¹³⁹, danazol¹⁴⁰, GnRH agonist therapy¹⁴¹, uterine nerve ablation by laparoscopy¹⁴², ablative laparoscopic surgery¹⁴³, and social support including endometriosis groups. Most of the medical treatments have been demonstrated to achieve pain relief in more than 75%⁹⁶. However, treatment of this condition is sometimes unrewarding owing to a lack of

effective interventions, and more radical surgery such as hysterectomy often becomes the final option¹⁴². It is the duty of medical staff to discuss the therapy plan with the patients.

Although pelvic pain, dysmenorrhea, dyspareunia, and infertility are considered typical symptoms of endometriosis, our respondents addressed other multiple and varied questions. Another finding documented by Denny et al.¹¹⁸ showed that delay in the diagnosis of endometriosis, pain, dyspareunia, and treatment were the identified key areas of discussions. Severe pain was often described as intense or overwhelming¹¹⁸. Cox¹⁴⁴ reported that the lack of support, the struggle, the losses involved in living with endometriosis, and trivialization of symptoms were the main findings from 61 women facing laparoscopy for endometriosis.

The findings of this study addressed a gap in the research literature about the information needs of women with endometriosis. Most of the mentioned literature may be limited by the number of respondents. They were asked passively, either by personal interview or by telephone. This study had brought a large number of respondents addressing the questions actively, freely and without limitation.

The study had several limitations. Multiple questions were addressed at the same time and most of all contained different topics. We summarized only the core of the letters. Therefore the summary did not reflect the consultation letters completely. Other points of view from these letters are not less important.

Future directions of research studies should be undertaken, particularly in the area of discussion forums for endometriosis. Diagnosis of endometriosis among the respondents should be collected, and the form of the question should be standardized.

Internet questionnaires

The primary outcomes studied were the six domains of endometriosis – chronic pelvic pain, dysmenorrhea, dyspareunia, hematochezia or hematuria, infertility, use of oral contraceptives and the relationship with six social impacts – quality of life, sexual activity, physical activity, productivity, working activity, and lost of working time. A

multidimensional scale was developed by Biberoglu and Behrman¹⁴⁰ and has been widely used in many interventional studies. In this scale, symptoms of dysmenorrhea, dyspareunia, pelvic pain were scored by the patients and the physical findings of pelvic tenderness and indurations were scored by the physician. The sums of these variables comprised the Total Pelvic Symptom Score (TPSS)¹⁴⁰. From an estimated 5 to 7 million women with endometriosis, 2 to 5 million experience pain, 200,000 to 800,000 infertility and 100,000 to 200,000 endometriomas¹. Infertility and pain cause a serious disruption of life as well as psychological sequels. In our study, questions were formulated to be easily understandable and without bringing any confusion. Therefore the questions were answered by simple options. Scoring was performed according to the study of Dr. Bühler et al. (unpublished study). Up to now no available questionnaire can be used to diagnose endometriosis. Another English-based internet questionnaire with 44 points of questions was placed by the Endometriosis All Party Parliamentary Group (EAPPG) with support from the National Endometriosis Society UK in www.endometriosis.appg.org/survey.htm. In this questionnaire the diagnosis of endometriosis was asked for in detail, including the time of diagnosis, how the diagnosis of endometriosis was made, and also questions about misdiagnosis. In our questionnaire, the data of physical findings by the physician and information about the diagnosis of endometriosis were not collected.

A number of studies in the past few years have examined the association between chronic pelvic pain and quality of life. Some instruments with established disease-specific questionnaires have been developed to measure the health/quality of life of women with endometriosis^{145,146,147,148}. But these health or quality of life questionnaires were complicated and not applicable in the internet questionnaire. Therefore the social impact of the respondents' symptoms was classified as severe, moderate or absent.

Dysmenorrhea was reported by 97% of the respondents at different levels of frequency. Chronic pelvic pain was also reported by 71% of the respondents. Collectively, dysmenorrhea and chronic pelvic pain were reported by 7458 respondents (70%). Pain may occur in women without pelvic pathology, as even normal menstruation releases prostaglandins that contribute to the sensation of pain¹⁴⁹. Dysmenorrhea is reported in up to 50% of women, most of whom do not have pelvic pathology¹⁵⁰. In the literature, the prevalence of endometriosis among dysmenorrheal women was up to 76% and up to

45% among women with chronic pelvic pain. Dysmenorrhea itself is a common condition that occurs in 52%^{151,152}, 72%^{153,154,155} of women, respectively. Another study by Weissman¹⁵⁶ found that 77% of 404 women without endometriosis, pelvic inflammatory disease or uterine fibroids (female students and graduates of the College of Nursing) had dysmenorrhea of different severity. A summary of the characteristics of patients with endometriosis from different publications is shown in Table 11.2 - Appendix.

Weissman¹⁵⁶ found that oral contraception was not significantly associated with less severe dysmenorrhea. Our findings showed that less frequent dysmenorrhea was significantly associated with taking oral contraceptives ($p < 0.0001$). Previous studies have found that dysmenorrhea causes frequent absence from work in 5-14% of women and absence from school in 14-46% of adolescents. Weissman¹⁵⁶ reported also that 2% of the respondents had dysmenorrhea that was severe enough to warrant staying home in bed. In our study, always having dysmenorrhea during the menstrual bleeding caused a more frequent absence from work (more than 10 days per year) in 615 participants ($p < 0.0001$).

A public health study showed that active-duty patients required on average 15 days of sick leave per hospital admission related to endometriosis. For this reason the US Army had a policy to disqualify female recruits with a history of endometriosis¹⁵⁷. Another finding of Boling¹⁵⁸ revealed that the estimated loss of duty time was 21,746 days in the United States Army. Our findings showed that 296 (20%) respondents with the highest probability of having endometriosis reported disability for more than 10 days ($p < 0.0001$).

Table 5.1. Correlation of probability of endometriosis and days of disability

Category of sum score (probability of endometriosis)	Disability days (n=4815)		
	0 – 1 day	2 – 10 days	>10 days
0 – 3	9 (100%)	0 (0%)	0 (0%)
4 – 8	265 (72.40%)	71 (19.40%)	30 (8.20%)
9 – 15	1883 (63.04%)	777 (26.01%)	327 (10.95%)
16 – 24	653 (44.94%)	504 (34.69%)	296 (20.37%)
Pearson's chi square test:			$p < 0.0001$

The lack of diagnosis of endometriosis limited our study. Although www.endometriose.de presents mostly information about endometriosis, the viewers are not restricted to women with endometriosis. The Web page is opened for anyone who

has internet access. Therefore registration and password protection are needed. Future study should be aimed at finding the correlation between the questionnaire and the diagnosis of endometriosis. Developing an accurate scoring system for the questionnaire should be also examined in the future study.

Endometriosis Web sites

There are thousands of Web sites on endometriosis, and patients or women are unlikely to review pages and pages of a search to locate the best sites, even if they had the knowledge and skill to evaluate their quality. In evaluating health Web sites, the source of the information is considered a marker of quality, but the source does not guarantee that the information is relevant and comprehensive. Professional organizations, universities, and government agencies are considered reliable and credible sources of health information in the Web. Individual health care providers and organized groups of health care providers are clearly sources of authoritative medical information. And organizations such as consumer advocacy groups, voluntary health-related organizations, public health communities, and patient support organizations can also be considered credible sources of information relating to their area of expertise. Similarly, hospitals, large group practices and other entities that bring together medically knowledgeable professionals have aggregate credibility. And university medical schools may have the highest degree of medical credibility since they are expected to represent collections of specialized physicians who are the spearheads of medical knowledge. 45% of these Web sites have been developed by reputable sources such as foundations, government-affiliated organizations and health organizations. Regarding the quality of editorial content, most sites lacked descriptions of the editorial process (35%), the source of specific content (30%), and dates on posting (15%).

Due to the lack of a peer-review process, such as that used for medical journals, the validity of information on these Web sites is sometimes questionable. This evidence was in the form of research studies cited from medical publications, a list of references, or supporting statements from reputable organization such as the American Academy of Family Physicians and the National Endometriosis Society United Kingdom. The content of the information presented on a health Web site should be accurate and supported by evidence such as clinical trials. 16 (80 %) of the Web sites provided

evidence or expert opinion to support the information they presented in their homepage. Many included links to additional resources. www.endozone.org provided a direct link to additional information about newest clinical trials. Other sites included general resources to supplement the information of the page, such as links to the www.obgyn.net.

Most Web sites provided information about Web site ownership (80%), copyright and sponsorship of any specific content (55%). But most Web sites failed to provide information about restriction on access to content, including registration, password protection (45%), and payment (45%). These findings are consistent with a study by Huang¹⁵⁹. Although most Web sites were easy to navigate, features of site map, FAQ (frequently asked questions) are seldom found.

Another strategy to search health Web sites is to find the internet quality of control seals, for example, the HON seal of approval. In our study only 40% of the Web sites had this HON seal of approval. As the use of the internet continues to gain in popularity, more people are turning to Web sites for health information. However, there are still Web sites that promote particular products, and might give misleading information. In the latest report about the quality of fertility clinic Web sites, Huang¹⁵⁹ concluded that most of them did not routinely meet the AMA (American Medical Association) guidelines for Web sites. Our study showed that Web sites with the HON certificate had a significantly higher score than Web sites without the HON certificate.

There were 3 Web sites using prestigious sound-alike names to promote a product or service (Lupron Depot®, Progestelle and Endo-Fem® with PMS Plus®). Additionally, none of the sites evaluated here suggested any “amazing result”, “earthshaking breakthroughs”, or “miracle cures” for endometriosis.

www.endometriose.de met 16 criterions from a total of 26 points in this study. Some lacks of performance could be improved. Restriction of access by requesting password or registration could protect the information from computer freaks, Web hijackers or illegal copiers. Information about description of the editorial process, review process, and time of update or posting can increase credibility and competence.

6

CONCLUSION

Endometriosis is a chronic disease and one of the most common gynecologic conditions that have a physical and psychosocial impact on women. It was reported for the first time by Shroen in 1690 as “ulcer in peritoneal cavities”. Prior to Sampson’s metastatic theory in 1921, attention of research was focused on the molecular pathogenesis of endometriosis. Better understanding of the pathogenesis of the disease and precise molecular targets promise new effective and efficient treatments with minimal side effects. The efficacy of the latest treatments is still argued and controversial. Teaching patients about endometriosis and its treatment, providing written information, and sharing educational electronic resources may take place through the internet. It has well been characterized as disease without lobby since it lacks public awareness even though being one of the most frequent benign diseases in women. In order to provide adequate and easily accessible information for patients as well as health workers, an Internet Web site was created, www.endometriose.de that enables interested people to inform themselves and counsel free of charge on their endometriosis-associated problems.

The chance of pregnancy (19%) under diagnosis of endometriosis was the most frequently asked question. This core of question could be retrieved from totally 2202 internet consultations, which were sent between January 2002 and July 2004. Other main topics addressed were: diagnostic procedure, treatment of endometriosis associated pain, and hormonal therapies. Side effects of the medical treatment, surgical therapies and alternative therapies occurred less frequently as well as question considering recurrence and disease follow up. The distribution of dysmenorrhea in our population was 97% and chronic pelvic pain 71% as well. Dyspareunia alone has no direct cause of infertility ($p>0.0001$). The severity of the endometriosis-associated symptoms increases significantly with the reduction of social impact in terms of quality of life, sexual activities, physical activities, productivities, impairment days and annual absent days ($p<0.0001$). 6.1% of our respondents have the most endometriosis-associated symptoms and need more than 10 days absence from work per year.

As the use of the internet continues to gain in popularity, more people are turning to Web sites for health information. Persons using the Internet for searching health information are better informed after reading, interactive tasks, and virtual consultation. However, there are still some Web sites, which deliver inaccurate information, promotion and marketing that can misguide the whole information. With major search engine, more than 900.000 Web sites about endometriosis were found. But only 30% of them were categorized as good Web sites. 40% of these Web sites had a HON seal of approval. Our study showed that Web sites with the HON certificate had a significantly higher score than Web sites without the HON certificate. Therefore, a HON certificate could help the visitors to evaluate the quality of the Web sites. Health provider should be prepared to answer questions and offer suggestions for Internet based health resources.

Data collected from the www.endometriose.de interactive platform enable us to inform health insurance companies, politicians, and doctors about the needs of endometriosis patients. If a computer is online and available in the health setting for the education of patients, Web sites can be bookmarked for use by patients while waiting for their appointment with the doctor.

7

SUMMARY

Women with chronic pelvic pain, infertility and dysmenorrhea try to search for help about their problems. Although the most important symptoms of endometriosis are chronic pelvic pain, infertility, dysmenorrhea and dyspareunia, laparoscopic assessment in combination with histological examination remains the gold standard for the definitive diagnosis of endometriosis. The lack of information about these problems is accompanied by both uncertainty and emotional distress. Since the information should be easily accessible, an internet platform was developed by the EEIC allowing extensive information on endometriosis and also providing a so-called “Endo-Test” as well as an open discussion forum. The needed information of endometriosis was studied through discussion forum and the endometriosis-associated symptoms and social impacts were collected through an internet questionnaire. The data were collected in an interval of time. Discussion forum were limited from January 2002 until July 2004. 2202 internet consultations were identified and analyzed. 10665 questionnaires were filled out from July 2003 to July 2004. 20 internet Web sites about endometriosis were evaluated based on criterion, which were published by Huang et al.

Women with pelvic pain, dysmenorrhea, infertility, and dyspareunia need more information about fertility, diagnosis of endometriosis, pain treatment, followed by tailoring of hormonal therapy, and follow-up after surgical therapy.

71% of our studied population (7616 of 10665 respondents) had chronic pelvic pain and the prevalence of chronic pelvic pain among our total visitor was 3.2% (7616 of 241,393). Extensive chronic pelvic pain was reported by up to 43% of the respondent. The distribution of dysmenorrhea was 97% (10332 of 10665 respondents) and the prevalence of dysmenorrhea among studied population (10332 of 241,393) was 4.3%. The distribution of dyspareunia was 61% (6479 of 10665 respondents) and the prevalence of dyspareunia among studied population (6479 of 241,393) was 2.7%. The distribution of infertility was 39% (4179 of 10665 respondents) and the prevalence of infertility among our visitors (4179 of 241,393) was 1.7%.

Quality of life was significantly reduced by a more frequent dysmenorrhea and higher endometriosis score ($p < 0.0001$). The majority of respondents (51%) reported about extremely reduced quality of life.

Productivity was significantly reduced with a higher endometriosis score ($p < 0.0001$).

Up to 50% from the respondents had an extreme limited productivity.

More than 10 disability-days from work per year were reported by 296 (6.1%) respondents with the highest endometriosis score.

27.2% (2906 respondents) having the highest endometriosis score could be suspected to have endometriosis. Further study should be aimed at finding the correlation between the questionnaires and the diagnosis of endometriosis.

Information about definition, pathogenesis, symptoms, diagnosis, treatment, rehabilitation of endometriosis and also supportive therapy inclusive self-help group, chat room, online consultation can be found on the internet. The source of information is considered a marker of quality, but the source does not guarantee that the information is relevant and comprehensive.

Web sites such as familydoctor.org, www.endocenter.org, www.endozone.org, www.endometriose.de meet the standard criteria. The HON certificate could help the visitors to evaluate the quality of the Web sites. Professional organizations, universities, and government agencies are considered reliable and credible sources of health information on the Web. Standardization and certification could help the patients or internet surfers to find and evaluate the Web sites by themselves.

Keywords: endometriosis, social impacts, internet consultation, Web sites.

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10

ABBREVIATIONS

AFS: American Fertility Society
 AMA: American Medical Association
 ANOVA: Analysis Of Variance
 CA-125: Cancer Antigen-125
 CSV: Comma-Separated Values
 EAPPG: Endometriosis All Party Parliamentary Group
 EEIC: Europäisches Endometriose Informations-Centrum
 ENT: Ear-Nose-Throat
 FSH: Follicle Stimulating Hormone
 GnRH: Gonadotropin-Releasing Hormone
 HITI: Health Information Technology Institute
 HON: Health on the Net
 HTML: Hypertext Markup Language
 IVF: In Vitro Fertilization
 JLU Giessen: Justus Liebig Universität Giessen
 LH: Luteinizing Hormone
 MPA: Medroxy-Progesterone Acetate
 MRI: Magnetic Resonance Imaging
 MSN: Microsoft Network
 NK cells: Natural Kill cells
 ppt: parts per trillion
 SD: Standard Deviation
 SPSS: Statistical Package for the Social Sciences
 TCDD: 2,3,7,8-TetraChloroDibenzo-p-Dioxin
 TCM: Traditional Chinese Medicine
 TNF- α inhibitor: Tumor Necrosis Factor - α inhibitor
 TPSS: Total Pelvic Symptom Score
 TXT: text
 URAC's: Utilization Review Accreditation Commission
 URL: Uniform Resource Locator

11

APPENDIX

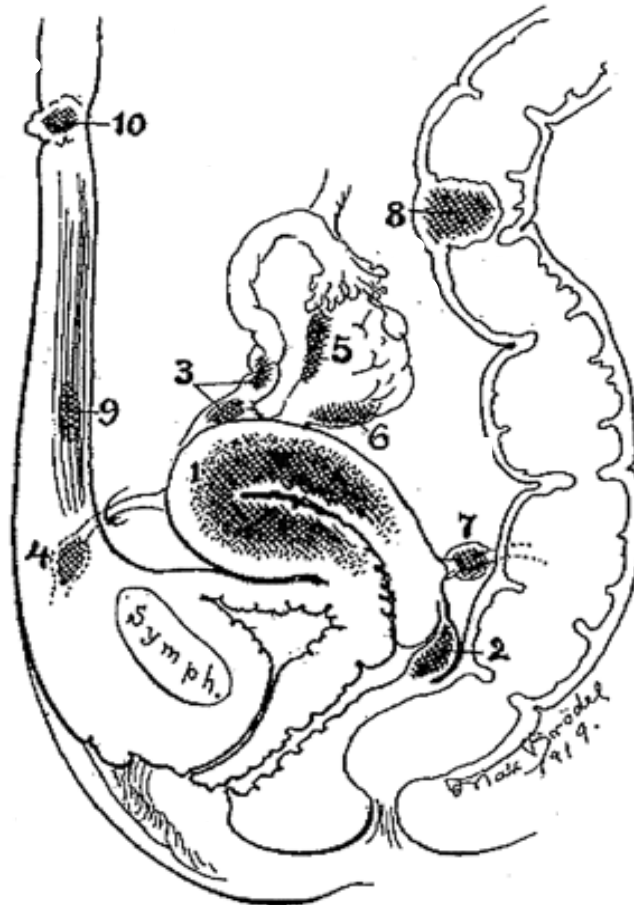


Figure 11.1. Cullen's diagram illustrating the distribution of adenomyomata

Table 11.1. Prevalence of endometriosis in different ethnic groups according to symptoms or operations

Symptoms/operations	Ethnic groups			
	African indigenous (%)	African-American (%)	Caucasian (%)	General (%)
Asymptomatic	-	-	-	2-22 ^[34,35,72]
Tubal ligation	-	-	6 ^[171]	4.1 ^[34]
Pelvic pain	-	-	15 ^[171] 45 ^[72]	24 ^[34]
Infertility	1.8 ^[161] 1.4 ^[162] 2 ^[163]	2.6 ^[166]	4.7 ^[166] 13-33 ^[172] 21 ^[171] 30 ^[72]	20 ^[34] 20-30 ^[72,173,174]
Infertility/pain/abnormal bleeding/benign gynecology	-	65 ^[167] 23 ^[168]	15 ^[167] 35 ^[72]	-
Hysterectomy	-	9 ^[169]	20 ^[169] 25 ^[171]	-
Gynecological surgery excluding laparoscopy	0.2 ^[164] 0.4 ^[165]	6.9 ^[170]	7.7 ^[170]	-
Dysmenorrhoea	-	-	-	40-60 ^[72,173,174]

* Numbers in brackets correspond to references

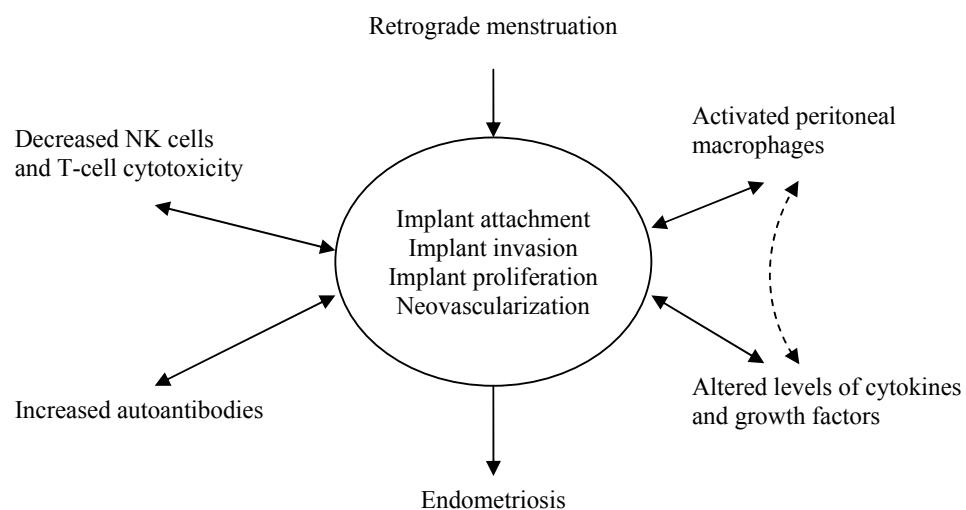


Figure 11.2. Immune alterations and endometriosis (Adapted from Berkkanoglu and Arici)⁴⁷

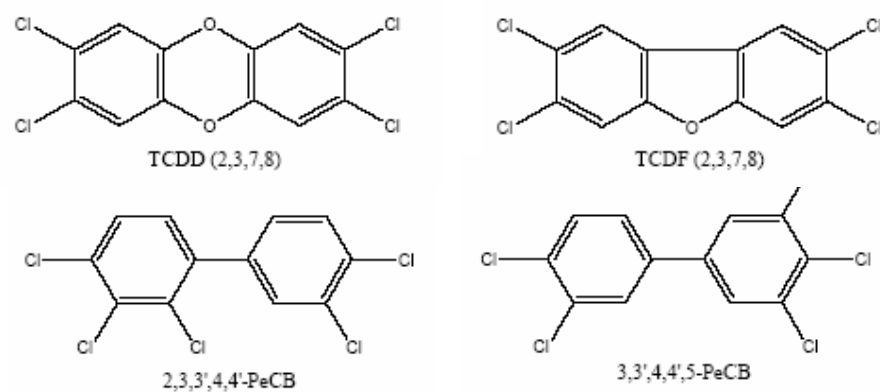


Figure 11.3. Dioxins and related congeners

Table 11.2. Characteristics of patients with endometriosis

	(n=339) ^[36]	(n=80) ^[175]	(n=187) ^[175]	(n=357) ^[176]	(n=336) ^[176]	(n=1542) ^[177]	(n=705) ^[156]	(n=404) ^[156]	(n=235) ^[177]	(n=126) ^[62]	(n=2777) ^[178]
Age at diagnosis											
Mean (years)	32.3 ± 7.4	25.6 ± 6.7	28.0 ± 7.1	32.6 ± 6.9	33.8 ± 4.8	34 ± 6.7	-	-	38.2 ± 9.2	-	37.3 ± 6.4
10-19	5 (1.5%)	-	-	10 (2.8%)	0 (0%)	-	-	78 (19%)	27 (11%)	25 (19.8%)	-
20-29	134 (39.5%)	-	-	107 (30%)	64 (19%)	-	-	175 (43%)	120 (51%)	33 (26.2%)	338 (12%)
30-39	135 (39.8%)	-	-	182 (51%)	226 (67.3%)	-	-	-	65 (28%)	41 (32.5%)	1563 (56%)
40-49	63 (15.6%)	-	-	58 (16.2%)	46 (13.7%)	-	-	151 (37%)	20 (9%)	27 (21.4%)	876 (32%)
50-59	2 (0.6%)	-	-	-	-	-	-	-	3 (1%)	-	-
Chief complaints											
Bowel or bladder symptoms	-	22 (28%)	60 (32%)	-	-	-	-	-	-	Tubal sterilization	Asymptomatic: 18%
Dysmenorrhea	217 (64.0%)	61 (76%)	133 (71%)	-	-	-	-	-	-	80 (64.5%)	-
Abdominal pain	102 (30.1%)	56 (70%)	132 (71%)	238 (67%)	-	24 (15%)	540 (76%)	301 (74.5%)	115 (49%)	-	46%
Infertility	76 (22.4%)	12 (15%)	37 (20%)	-	178 (53%)	133 (21%)	-	-	64 (27%)	-	55%
Ovarian mass	-	22 (28%)	25 (13%)	-	-	-	-	-	-	-	47%
Dyspareunia	-	22 (28%)	25 (13%)	-	-	-	-	-	-	-	-
Menarche	-	35 (44%)	83 (44%)	-	-	-	-	-	45 (19%)	-	-
Mean (years)	12.2 ± 1.2	12.8 ± 1.5	12.6 ± 1.5	-	-	12.54 ± 1.53	12.6 ± 1.4	12.6 ± 1.3	-	-	-
Cycle length											
Mean (days)	27.1 ± 3.7	28.4 ± 3.2	27.8 ± 3.5	-	-	-	-	-	-	≤29d: 66 (52.4%)	-
										≥30d: 58 (46.0%)	-
										1-4d: 68 (54.8%)	-
										5-6d: 45 (36.3%)	-
										≥7d: 11 (8.7%)	<27d: 501 (18%)
Menstruation duration											
Mean (days)	6.0 ± 1.4	6.0 ± 1.8	6.4 ± 1.9	-	-	-	-	-	-	-	-
Marital status											
Married	246 (72.6%)	24 (31%)	105 (57%)	-	-	-	452 (64%)	265 (66%)	-	94 (75.2%)	-
Single	93 (27.4%)	52 (68%)	73 (40%)	-	-	-	196 (28%)	115 (28%)	-	31 (24.8%)	-
Divorced	-	1 (1%)	6 (3%)	-	-	-	56 (8)	23 (6%)	-	-	-
No. of live births											
Nulliparous	142 (57.7%)	64 (80%)	118 (63%)	-	-	-	260 (39%)	152 (40%)	-	23 (18.3%)	-
Live Birth – 1 or more	104 (42.3%)	16 (20%)	69 (37%)	-	-	-	400 (57%)	229 (57%)	-	103 (81.7%)	-
Family history											
Endometriosis	22 (8.8%)	25 (33%)	40 (26%)	-	-	-	-	-	-	-	-
Breast cancer	-	24 (31%)	31 (19%)	-	-	-	-	-	-	-	-
Endometrial cancer	-	4 (5%)	4 (2)	-	-	-	-	-	-	-	-
Melanoma	-	11 (14%)	16 (10)	-	-	-	-	-	-	-	-
Ovarian cancer	-	3 (4%)	11 (7)	-	-	-	-	-	-	-	-
Smoking	-	-	-	-	-	-	-	39 (9.7%)	-	36 (28.6%)	968 (35%)

* Number in brackets corresponds to references

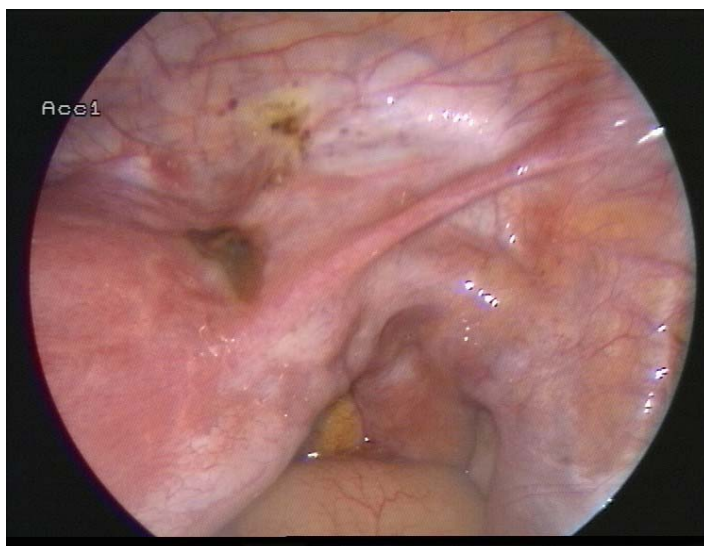


Figure 11.4. Peritoneal implant of endometriosis at bladder peritoneal surface

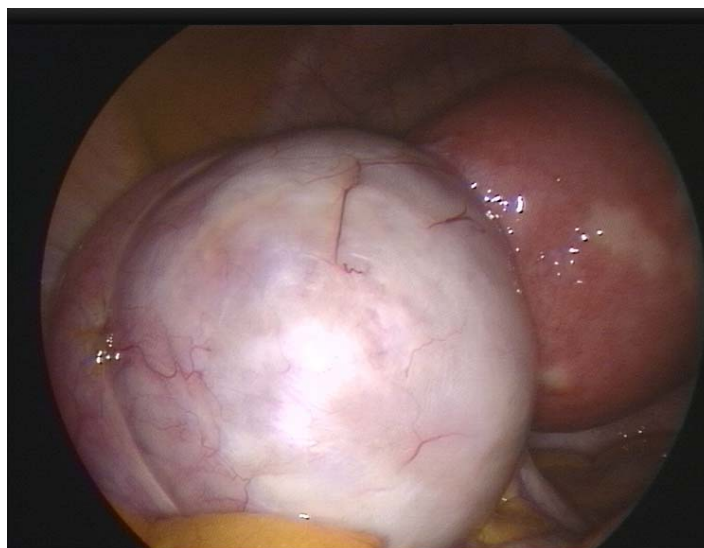


Figure 11.5. Endometrioma appearances (4 cm) in laparoscopic assessment (31-year-old patient with recurrent endometriotic cyst and abdominal pain)

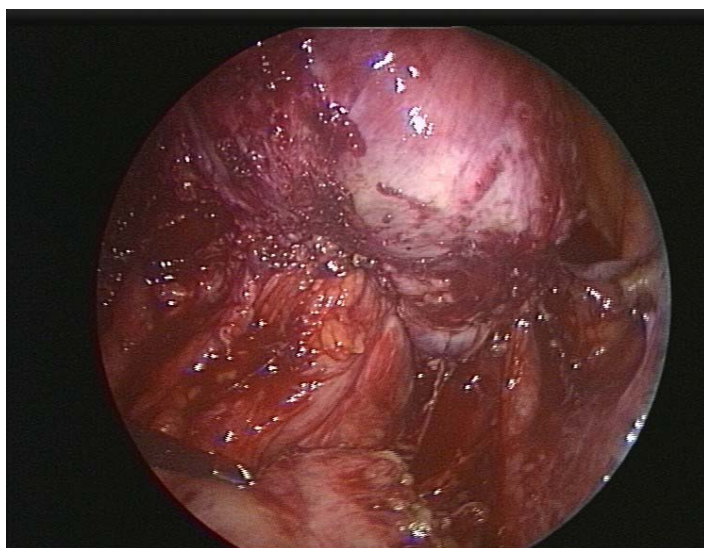


Figure 11.6. Deep infiltrating endometriosis

Table 11.3. Markers for endometriosis⁸⁷

Tumor markers and polypeptides
a. CA-125, CA-19-9
b. SICAM-1 (soluble forms of the intercellular adhesion molecule-1)
c. Glycodelin-A (PP 14)
Immunological markers
a. Cytokines: IL-6, TNF
b. Autoantibodies
1. Antiendometrial
2. Autoantibodies to markers of oxidative stress
Genetic markers
a. Early growth response (EGR)-1 gene
b. P450 aromatase
c. Placental protein 14 (PP14)
Tissue markers
a. Aromatase P 450
b. Cytokeratins
c. Hormone receptors

* Adapted from Bedaiwy⁸⁷Table 11.4. Surgical principles in the treatment of endometriosis¹⁰³

Knowledge of disease and treatment modalities
Experienced surgeon
Adequate facilities, personnel, and equipment
Appropriate patient selection
Informed consent
Proper patient position
Careful pelvic evaluation
Maximum exposure
Use of magnification
Minimum tissue trauma
Excellent haemostasis
Removal of all diseased tissue
Avoidance of foreign body material
Confirmation through pathology

* Adapted from Adamson¹⁰³



AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE REVISED CLASSIFICATION OF ENDOMETRIOSIS

Patient's Name _____ Date _____
 Stage I (Minimal) - 1-5 Laparoscopy _____ Laparotomy _____ Photography _____
 Stage II (Mild) - 6-15 Recommended Treatment _____
 Stage III (Moderate) - 16-40 Prognosis _____
 Stage IV (Severe) - >40
 Total _____

PERITONEUM	ENDOMETRIOSIS	<1cm	1-3cm	>3cm
	Superficial	1	2	4
OVARY	Deep	2	4	6
	R Superficial	1	2	4
	Deep	4	16	20
	L Superficial	1	2	4
POSTERIOR CULDESAC OBLITERATION	Partial	Complete		
	4	40		
OVARY	ADHESIONS	< 1/3 Enclosure	1/3-2/3 Enclosure	> 2/3 Enclosure
	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
TUBE	Dense	4	8	16
	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
TUBE	Dense	4	8	16

*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.

Denote appearance of superficial implant types as red (R), red, red-pink, flame-like, vesicular blobs, clear vesicles), white (W), opacifications, peritoneal defects, yellow-brown), or black (B) black, hemosiderin deposits, blue). Denote percent of total described as R____%, W____% and B____%. Total should equal 100%.

Additional Endometriosis: _____ Associated Pathology: _____

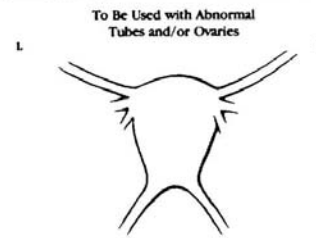
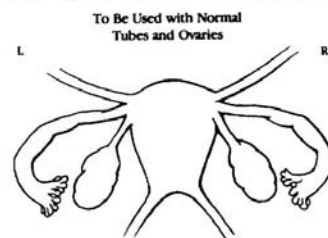


Figure 11.7. Revised Classification of endometriosis from ASRM 1996⁸⁹

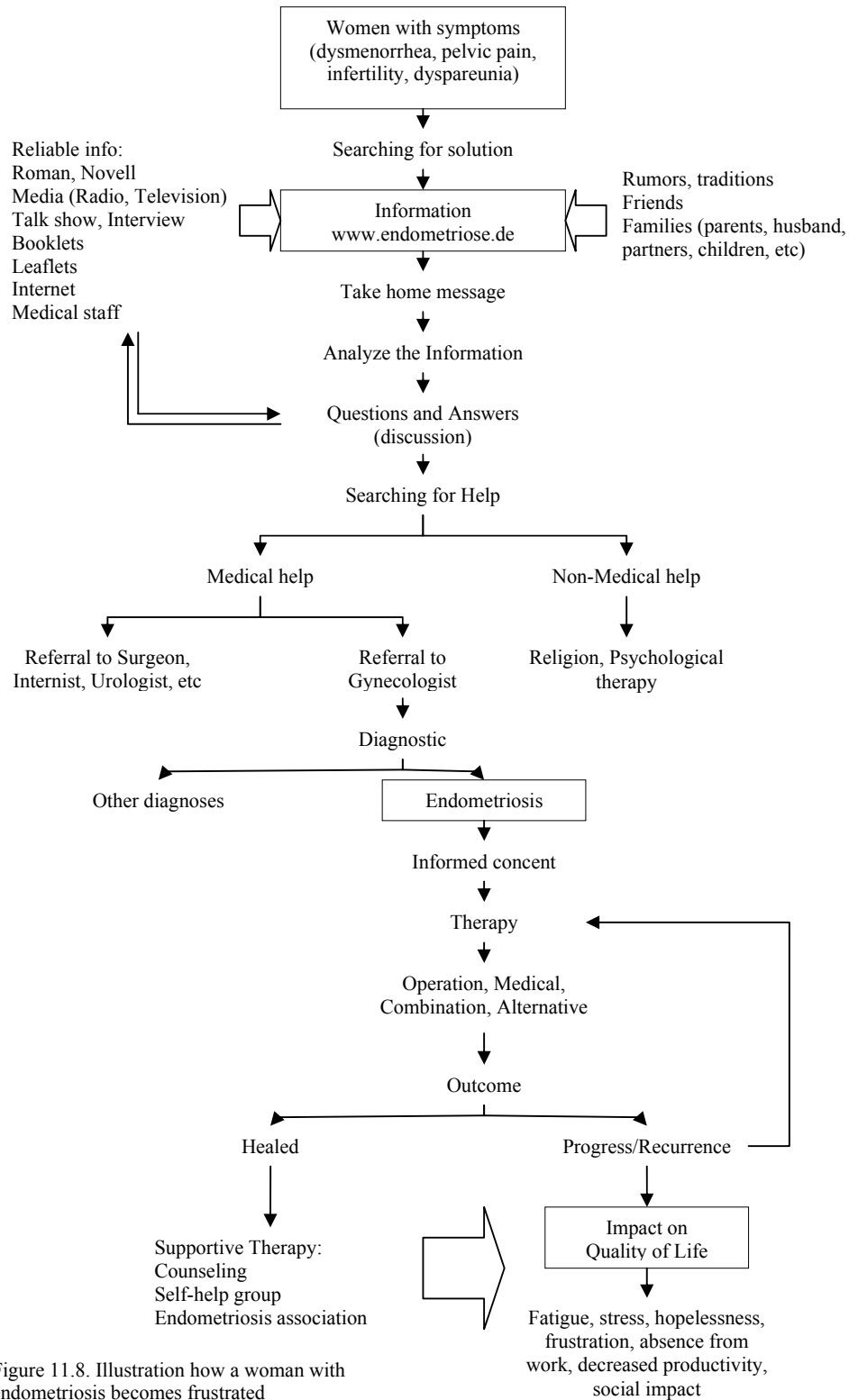


Figure 11.8. Illustration how a woman with endometriosis becomes frustrated

Table 11.5. Endo-Test, originally in German, translated by the author

	Points	
1. Do you have painful periods?		
a. always	3	<input type="text"/>
b. sometimes	2	
c. seldom	1	
d. never	0	
1.1. If yes, when does the pain begin in your period?		
a. days before the bleeding	2	<input type="text"/>
b. during the time of bleeding	1	
1.2. If yes, when do you have the most pain?		
a. before the bleeding	1	<input type="text"/>
b. together with the bleeding	2	
1.3. If yes, have you had this pain since the first time you had your period?		
a. yes	2	<input type="text"/>
b. no	1	
2. Do you have lower abdominal pain monthly without having any menstrual period and you do not have any gastrointestinal problem?		
a. often	3	<input type="text"/>
b. sometimes	1	
c. never	0	
2.1. If yes, is this pain very deep and strong or only mild?		
a. very strong	2	<input type="text"/>
b. mild	1	
3. Do you also have pain during intercourse?		
a. yes	1	<input type="text"/>
b. no	0	
3.1. If yes, does it depend on the position at intercourse?		
a. yes	1	<input type="text"/>
b. no	0	
3.2. If yes, where is the center point of this pain?		
a. deep vagina	3	<input type="text"/>
b. in the pelvic region	1	
c. at the entrance of the vagina	0	

4. Do you also have bleeding with urination and bowel movement before or during menstruation?		
a. yes	2	<input type="text"/>
b. no	0	
5. Do you have infertility problems?		
a. yes	2	<input type="text"/>
b. no	0	
6. Are you currently taking any contraceptives?		
a. yes	1	<input type="text"/>
b. no	0	
7. Does the pain reduce your quality of life?		
a. extremely	0	<input type="text"/>
b. mildly	0	
c. no change	0	
8. Does the pain reduce your sexual activity?		
a. extremely	0	<input type="text"/>
b. mildly	0	
c. no change	0	
9. Does the menstrual pain limit your physical activity?		
a. extremely	0	<input type="text"/>
b. mildly	0	
c. no change	0	
10. Do you feel that your productivity is limited because of the pain?		
a. extremely	0	<input type="text"/>
b. mildly	0	
c. no change	0	
11. How many days does the period pain limit your working activity?		
a. >3 days	0	<input type="text"/>
b. 1-3 days	0	
c. 0 day	0	
12. How many days in a year have you been unable to go to work?		
a. >10 days	0	<input type="text"/>
b. 2-10 days	0	
c. 0-1 day	0	
Total of points =		<input type="text"/>

Table 11.6. Delay in diagnosis of endometriosis

Literature	Delay in diagnosis of endometriosis (years)		
	Pelvic pain	Infertility	Total
Ballweg (2004) ¹¹⁷	-	-	>9
Husby et al. (2003) ¹¹⁶	6.7 ± 6.2	-	-
Arruda et al. (2003) ¹⁷⁹	7.4	4.0	7.0
Dmowski et al. (1997) ¹⁷⁶	6.35	3.13	-
Hadfield et al. (1996) ¹⁸⁰	11.73 ± 9.05 (USA)	-	-
	7.96 ± 7.92 (UK)		

Table 11.7. List of experts of www.endometriose.de

1. Prof. Dr. med. H-R Tinneberg, Giessen
2. Dr. med. Klaus Bühler, Langenhagen
3. Dr. med. Edgar Dewitt, Köln
4. PD Dr. med. Dr. phil. Andreas Ebert, Berlin
5. Prof. Dr. med. Göretzlehner, Torgau
6. Prof. Dr. med. Joerg Keckstein, Villach
7. Dr. med. Istvan Kocsis, Bonn
8. Prof. Dr. med. Lilo Mettler, Kiel
9. PD Dr. med. Michael Mueller, Bern
10. PD Dr. med. P.-A. Regidor, Münster
11. Prof. Dr. med. Thomas Römer, Köln
12. Prof. Dr. med. A.E. Schindler, Essen
13. Prof. Dr. med. Karl-Werner Schweppe, Westerstede
14. PD Dr. med. Martin Sillem, Aschaffenburg

Table 11.8. Number of visitors per month

September 2004	4234
August 2004	15587
July 2004	15262
June 2004	16113
May 2004	16709
April 2004	16475
March 2004	17809
February 2004	14858
January 2004	23390
December 2003	16190
November 2003	12667
October 2003	11422
September 2003	10639
August 2003	10093
July 2003	13444
June 2003	12872
May 2003	13629

Table 11.9. Correlation between probability of endometriosis with social impact

Category of sum score (probability of endometriosis)	Quality of life (%)			Sexual activity (%)			Physical activities (%)			Productivity (%)			Impairment days (%)		
	Absent	Moderate	Severe	Absent	Moderate	Severe	Absent	Moderate	Severe	Absent	Moderate	Severe	0 day	1 – 3 days	>3 days
0 – 3	55.56	33.33	11.11	66.67	22.22	11.11	100	0	0	88.89	11.11	0	66.67	33.33	0
4 – 8	27.10	40.65	32.25	58.70	26.09	15.21	20.82	38.08	41.10	27.72	35.33	39.95	25.34	62.94	11.72
9 – 15	13.80	40.38	45.82	32.00	39.97	28.03	11.50	33.36	55.14	16.97	36.44	46.59	13.80	68.01	18.19
16 – 24	3.68	28.75	67.57	7.38	34.38	58.24	3.02	23.47	73.51	4.92	33.15	61.93	5.57	57.04	37.39
Chi square test	p<0.0001			p<0.0001			p<0.0001			p<0.0001			p<0.0001		

Table 11.10. Web site criteria*

Website addresses	1.1	1.2	1.3	1.4	1.5	1.6	1.7	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	3.1	3.2	3.3	3.4	3.5	3.6	3.7	3.8	3.9	3.10	3.11	Σ
www.endometriosis.org (a)	0	1	0	0	1	1	1	1	0	1	1	0	0	0	1	1	0	1	1	1	1	1	0	1	0	1	15
www.hegresources.com/endoindex.html **(a)	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	1	1	22
familydoctor.org/handouts/476.html **(d)	1	1	0	0	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	0	1	1	20
www.ivf.com/endohtml.htm **(c)	1	0	0	0	1	0	1	0	1	0	0	0	0	0	0	0	1	1	0	1	0	0	1	0	1	1	10
www.womensurgerygroup.com/conditions/endometriosis/overview.asp **(c)	1	0	0	0	0	1	1	1	0	1	0	1	0	0	0	0	1	1	1	0	1	0	1	1	1	1	12
www.endometriospaintreatment.com (b)	0	0	1	0	1	1	1	0	1	0	0	0	0	0	0	0	1	1	1	1	1	0	1	0	0	0	10
www.womensendosurgery.com/endometriosis.html (c)	1	1	0	0	0	0	1	0	1	0	1	0	0	1	0	0	1	1	1	0	1	0	0	0	0	0	9
www.emedicine.com/emer/topic165.htm **(b)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0	1	0	22
www.endofacts.com (b)	1	0	1	0	0	1	0	0	1	0	0	0	0	1	0	0	1	1	1	1	1	1	0	1	0	1	13
www.endocenter.org **(a)	1	1	1	1	1	1	1	1	1	0	1	0	0	1	0	1	1	1	1	1	1	1	0	1	1	1	21
www.endozone.org or www.endometriosiszone.org **(a)	1	1	1	1	1	1	1	1	1	0	1	1	0	1	0	1	0	1	1	1	1	1	0	1	1	1	21
endometriosis.allbio.org (f)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
www.endometriosisasn.org (a)	1	0	1	1	1	1	1	0	1	0	1	0	0	1	0	0	1	1	1	1	1	1	0	0	1	0	15
www.centerforendo.com (c)	1	1	0	0	0	1	1	0	1	0	1	0	0	0	0	0	1	1	1	0	0	1	1	0	1	1	13
www.nlm.nih.gov/medlineplus/endometriosis.html (e)	1	1	1	1	1	1	1	1	1	0	1	0	0	1	0	1	1	1	1	1	1	1	0	1	1	1	21
www.endo.org.uk (e)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	0	0	1	21
www.endo101.com/index.htm (b)	1	0	1	1	1	1	1	0	1	0	1	0	0	0	0	0	1	1	1	1	1	1	0	0	1	0	15
www.endometriosis.com (b)	0	1	0	0	0	0	0	0	1	0	0	0	1	1	1	0	1	1	1	0	1	0	0	1	0	0	9
www.womenshealthchannel.com/endometriosis/index.shtml **(b)	1	1	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	6
www.endometriose.de (a)	1	0	1	1	1	1	1	1	1	1	1	1	0	0	0	1	1	1	1	1	0	0	1	0	1	0	17
www.endometriose.de (a)	1	0	0	0	0	1	1	0	1	0	1	0	0	1	0	0	1	1	1	1	1	1	1	1	1	1	16

* Criteria details see Table 11.11

** HON Certificate

! Letter in brackets corresponds to ownership of the Web sites: a. Foundation; b. Private company; c. Private clinics; d. Health organization; e. Government; f. Unknown

Table 11.11. Evaluation criteria in assessing endometriosis websites¹⁵⁹**1. Ownership and affiliations**

1. Website ownership, including affiliations, strategic alliances, and significant investors, should be clearly indicated on the home screen or via a directly accessible link on the home screen.
2. Copyright ownership of specific content should be clearly indicated.
3. Information about restrictions on access to content, required registration, and password protection, if applicable, should be provided and easy to find.
4. Information about payment subscriptions, document delivery, and viewing should be provided and easy to find.
5. Information about privacy should be provided and easy to find.
6. Funding or other sponsorship for any specific content should be clearly indicated.
7. Content should be easily distinguishable from advertising.

2. Editorial content

1. Content should be reviewed for quality (including originality, accuracy, and reliability) by either peer review or editorial boards.
2. The language complexity of the content should be appropriate for the site's audience.
3. A description of the editorial process and method of content review should be posted on the site.
4. All staff members and other individuals (i.e., editorial board) responsible for content quality should be posted on site.
5. The dates on which content is posted, revised, and up-dated should be clearly indicated.
6. Sources for specific content should be clearly identified (i.e., author byline or names of individual, organization, department, institution, agency, or commercial provider/producer).
7. Affiliations and relevant financial disclosures for authors and content producers should be clearly indicated.
8. Reference material used to develop content should be cited in a manner appropriate for the site's audience.

3. Navigation

1. The website should provide information about the platform(s) and browser (that permit optimal viewing in a location that is easy to find).
2. The intrasite content links should be functional.
3. The external links should be functional.
4. The website allows viewers to return to previously browsed websites.
5. The website does not redirect viewer to unintended websites.
6. Information on portable document format (PDF) files and software download instruction should be provided and easy to find.
7. The website features include a site map.
8. The website features include a "frequently asked questions" (FAQ) page.
9. The website features include a feedback mechanism.
10. The website features include customer service information.
11. Each distinct site should provide a search engine with instructions specifying how to use the search function.

Table 11.12. Evaluation criteria in assessing endometriosis websites		
Criteria	Fulfilled	Percentage (%)
Ownership and affiliations		
1. Website ownership, including affiliations, strategic alliances, and significant investors, should be clearly indicated on the home screen or via a directly accessible link on the home screen.	16	80
2. Copyright ownership of specific content should be clearly indicated.	11	55
3. Information about restrictions on access to content, required registration, and password protection, if applicable, should be provided and easy to find.	9	45
4. Information about payment subscriptions, document delivery, and viewing should be provided and easy to find.	9	45
5. Information about privacy should be provided and easy to find.	11	55
6. Funding or other sponsorship for any specific content should be clearly indicated.	15	75
7. Content should be easily distinguishable from advertising.	16	80
Editorial content		
1. Content should be reviewed for quality (including originality, accuracy, and reliability) by either peer review or editorial boards.	7	35
2. The language complexity of the content should be appropriate for the site's audience.	18	90
3. A description of the editorial process and method of content review should be posted on the site.	7	35
4. All staff members and other individuals (i.e., editorial board) responsible for content quality should be posted on site.	13	65
5. The dates on which content is posted, revised, and up-dated should be clearly indicated.	3	15
6. Sources for specific content should be clearly identified (i.e., author byline or names of individual, organization, department, institution, agency, or commercial provider/producer).	6	30
7. Affiliations and relevant financial disclosures for authors and content producers should be clearly indicated.	10	50
8. Reference material used to develop content should be cited in a manner appropriate for the site's audience.	4	20
Navigation		
1. The website should provide information about the platform(s) and browser (that permit optimal viewing in a location that is easy to find).	8	40
2. The intrasite content links should be functional.	17	85
3. The external links should be functional.	18	90
4. The website allows viewers to return to previously browsed websites.	14	70
5. The website does not redirect viewer to unintended websites.	16	80
6. Information on portable document format (PDF) files and software download instruction should be provided and easy to find.	12	60
7. The website features include a site map.	5	25
8. The website features include a "frequently asked questions" (FAQ) page.	8	40
9. The website features include a feedback mechanism.	12	60
10. The website features include customer service information.	10	50
11. Each distinct site should provide a search engine with instructions specifying how to use the search function.	12	60

LEBENS LAUF

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Schulbildung

1982 – 1988 Christliche Grundschule Samaria
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 1988 – 1991 Christliche Mittelschule II (SMPK II)
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 1991 – 1994 Christliches Gymnasium I (SMAK I)
 Jakarta, Indonesien
 Abschluß : Hochschulreife

Berufsausbildung

1994 - 1998 Vorklinisches Studium
 Medizinische Fakultät Universität Indonesien
 Jakarta, Indonesien
 Abschluß : Sarjana Kedokteran (Bsc. Med.)

Praktisches Jahr

06.1998 – 12.1998	Innere Medizin 3 Monate Pädiatrie 3 Monate Zentrales Nationales Krankenhaus Ciptomangunkusumo – Klinikum der Universität Indonesien, Jakarta Städtisches Krankenhaus Tangerang, Jakarta Lehrkrankenhaus der Universität Indonesien
01.1999 – 07.1999	Dermato- und Venerologie Psychiatrie Klinische Pharmacologie Neurologie Radiologie Public Health (je Abteilung 1 Monat) Zentrales Nationales Krankenhaus Ciptomangunkusumo
08.1999 – 10.1999	Gynäkologie und Geburtshilfe Zentrales Nationales Krankenhaus Ciptomangunkusumo Städtisches Krankenhaus Tangerang
11.1999 – 02.2000	Rechts Medizin Ohr-Hals-Nasen Augenheilkunde Anästhesiologie (je Abteilung 1 Monat) Zentrales Nationales Krankenhaus Ciptomangunkusumo
03.2000 – 05.2000	Public Health Mutter- und Kinderklinik „Utan Kayu“ Familie Klinik „Kiara“ Jakarta, Indonesien
05.2000 – 08.2000	Chirurgie Zentrales Nationales Krankenhaus Ciptomangunkusumo Städtisches Krankenhaus Tangerang
08.2000	Abschluß des medizinischen Studiums : Arzt

Studienbegleitende Tätigkeiten

Zusatzqualifikationen

2000	Kurs „Advance Cardiac Live Support“ nach American Heart Association
2001	Kurs „Advance Trauma Life Support“ nach American College of Surgeons Committee on Trauma

EDV	MS Excel, Textbearbeitung (MS Word), MS Powerpoint, Design graphic (Adobe Illustrator), Access, Database, Photographie, Photobearbeitung, SPSS, Videobearbeitung, Webmeister
Sprachkenntnisse	Indonesisch – Muttersprache Deutsch – fließend Englisch – sehr gut
Forschung	„Die Verhalten und Kenntnisse der Mütter über Immunisation ihrer Kinder und die beeinflussenden Faktoren im Bezirk Matraman, Ost-Jakarta“ – 2000 „Die Verhalten und Kenntnisse der Frauen über Menopause und die beeinflussenden Faktoren im Bezirk Senen, Zentral-Jakarta“ – 2000

Kurse und Fortbildungen

02.2002	Fortbildung „Onkologische Fortbildungsveranstaltung der Projektgruppen des Tumorzentrums Tumornachsorge“, Erlangen
02.2002	Kurs „Doppler- und Farbdoppler-Sonographie in der Gynäkologie und Geburtshilfe“, Erlangen
03.2002	Fortbildung „Neues zur Therapie der Hypertonie bei Typ 2 Diabetes“, Erlangen
03.2002	Fortbildung „Aktuelles in der Prävention, Diagnostik und Therapie von zervikalen Dysplasien und des Zervixkarzinoms“, Erlangen
04.2002	Fortbildung „14. Erlanger Anästhesie-Seminar“, Erlangen
06.2002	Fortbildung „Mammakarzinom Früherkennung versus Screening“, Erlangen
06.2002	Fortbildung „Fortschritte in der Diagnostik und Therapie kardiovaskulärer Synkopen“, Herzogenaurach
07.2002	Fortbildung „Fortgeschrittenes Karzinom der Mamma“, Bayreuth
11.2002	Fortbildung „Gynäkologische Onkologie 2002 Leitlinien, medikamentöse Strategien und Studien“, Erlangen

11.2002	Fortbildung „ Grenzen der Reproduktionsmedizin “, Giessen
11.2002	Fortbildung „ Schilddrüse und Herz “, Erlangen
11.2002	Fortbildung „ Update Endometriose 2002 “, Erlangen
01.2003	Fortbildung „ Giessener Gynäkologische Fortbildung 2003 “, Gießen
02.2003	Fortbildung „ 36. Erlanger Fortbildungstage für Praktische Medizin “, Erlangen
03.2003	Fortbildung „ Perinataalkongress Frankfurt 2003 “, Frankfurt am Main
10.2003	Fortbildung „ Kontrazeption und Hormonsubstitution “, Mainz
11.2003	Fortbildung „ Kinderwunsch bei systemischen Erkrankungen “, Gießen
11.2003	Fortbildung „ 1. Brustkrebs-Symposium des Brustzentrum Mittelhessen “, Gießen
12.2003	Fortbildung „ Geburtshilfliche-Pädiatrischen Fortbildung “, Gießen
12.2003	Fortbildung „ Radio-Onkologisch-Gynäkologischen Fortbildung “, Gießen
03.2004	Fortbildung „ Moderne Kinderwunschbehandlung in regionaler Kooperation an einem IVF-Zentrum “ und „ Moderne Kontrazeptionsmethoden “, Herborn
05.2004	Fortbildung „ Der juristische Notfallkoffer “ und „ Modernes Thrombosemanagement “, Mannheim
06.2004	Fortbildung „ 5. Düsseldorfer Symposium Mammakarzinom-Behandlung – Eine multidisziplinäre Herausforderung “, Düsseldorf
07.2004	Fortbildung „ 203. Tagung Niederrheinisch-Westfälische Gesellschaft für Gynäkologie und Geburtshilfe (NWGGG) “, Köln
07.2004	Kurs „ Mammasonographie “, Köln

07.2004	Fortbildung „ Carcinoma in situ der Mamma / Interventionelle Diagnostik / Sentinel-Lymph-Node-Biopsie “, Bayreuth
10.2004	Fortbildung „ Molekulare Befunde bei der Endometriose “, Bad Nauheim
10.2004	Fortbildung „ Möglichkeiten, Grenzen und Videodemonstration minimal-invasiver Operationsverfahren “, Gießen
11.2004	Fortbildung „ Mammographie-Screening, Brustzentrum Mittelhessen “, Gießen
11.2004	Fortbildung „ Interdisziplinäre Andrologie und Reproduktionsmedizin “, Gießen
06.2005	Fortbildung „ 177. Tagung der Mittelrheinische Gesellschaft für Geburtshilfe und Gynäkologie (MGGG) “, Frankfurt am Main
07.2005	Fortbildung „ 1 st Endoscopy Meeting “, Gießen
07.2005	Kurs „ Sonographie-Grundkurs Schwangerschaftsdiagnostik: weiterführende Differentialdiagnostik des Feten – (B-Mode-Verfahren) “, Frankfurt am Main
09.2005	Fortbildung „ Gynäkologie Kompakt “, Frankfurt am Main
09.2005	Fortbildung „ IX. World Congress on Endometriosis “, Maastricht, the Netherlands
10.2005	Fortbildung „ Internationaler deutschsprachiger Kongress – Menstruation & Endometriose “, Villach, Österreich
11.2005	Kurs „ Psychosomatische Grundversorgung “, Weilburg

Praktische Tätigkeiten

08.00 – 08.01	Assistenzarzt der Frauenklinik Pluit Krankenhaus Jakarta, Indonesien
08.00 – 08.01	Allgemeinarzt Tedjo and Associate Clinics Jakarta, Indonesien

11.01 – 03.02	Stipendiat Frauenklinik der Universität Erlangen-Nürnberg Erlangen, Deutschland
04.02 – 02.03	Assistenzarzt Frauenklinik der Universität Erlangen-Nürnberg Erlangen, Deutschland
03.03 – jetzt	Assistenzarzt Frauenklinik der Universität Gießen-Marburg Standort Gießen, Deutschland

Publikationen

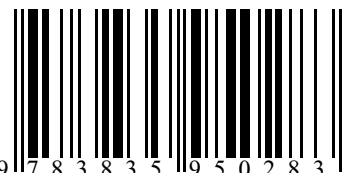
2005	Suwandinata F, Manolopoulos K, Tinneberg HR. www.endometriose.de - Result of internet survey and internet consultation about endometriosis. Abstract - European Journal of Obstetrics and Gynecology and Reproductive Biology 2005; 123(Suppl. 1): S28.
2005	Suwandinata F, Manolopoulos K, Tinneberg HR. Result of internet survey and internet consultation about endometriosis. Abstract - Zentralblatt für Gynäkologie 2005; 127(5): 353.
2005	Manolopoulos K, Suwandinata F, Tinneberg HR. Endometriose und Infertilität. Journal für Reproduktionsmedizin und Endokrinologie 2005; 2(5): 291-295.

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